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# Studies with Polyfunctionally Substituted Heteroaromatics: New Routes for the Synthesis of Polyfunctionally Substituted Pyridines and 1,2,4-Triazolo[1,5-a]pyridines

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## ABSTRACT

*The 1-substituted ethylidenemalononitriles* **1a–c** *condensed with triethyl orthoformate in refluxing acetic anhydride to yield the dienes* **2a–c**. *On the other hand, a mixture of N,N-dimethylformamide and triethyl orthoformate condensed with* **1a–d** *to yield the N,N-dimethylaminopentadienonitriles* **2d–g**. *The pentadienonitriles* **2d–g** *were also formed from the reaction of* **1a–d** *with dimethylformamide dimethylacetal in refluxing acetic acid. When compounds* **1a–c** *were treated with dimethylformamide dimethylacetal in refluxing p-xylene, a mixture of* **3,4** *and* **2e–g** *was formed.*

*The reaction of* **2a,b** *with hydrazine hydrate afforded the N-amino-2-iminopyridines* **5a,b**. *These were converted into the triazolo[1,5-a]pyridines* **8a–d** *on treatment with benzoyl chloride and with dimethylformamide dimethylacetal. On the other hand, the reaction of* **2c** *with hydrazine hydrate afforded the pyrazolo[3,4-b]pyridine* **7c**. *Treatment of* **2a,c** *or* **2e,g** *with cyanoethanoic hydrazide afforded the N-(cyanoacetamido)pyridines* **9a,b**. *The dienes* **2d,f,g** *afforded the pyridones* **11a–c** *on treatment with acetic acid and hydrochloric acid mixture. Compounds* **11b,c** *were also formed on treatment of* **2b,c** *with acetic acid hydrochloric acid mixture. The reaction of* **2d,g** *with ethanolic sodium ethoxide gave the ethoxypyridines* **13a,b**.


Substituted ethylidenemalononitriles **1** are readily obtained either by condensing active methylene nitriles with methyl or methylene ketones [1–3] or by dimerization of acetonitrile derivatives [4,5]. Methyl and methylene moieties in these molecules are highly active toward electrophilic reagents, and this activity has been extensively utilized in synthesis [6–8]. As a part of our program aimed at developing efficient syntheses of polyfunctional substituted aromatics utilizing simple and efficient procedures and relatively inexpensive starting materials, we have previously developed routes to polyfunctionally substituted azines utilizing derivatives of **1** as starting materials [9–12]. Our synthetic routes have been utilized extensively [13–15], and this encouraged us to explore further the potential of **1** in heterocyclic synthesis. The work enabled synthesis of several new polyfunctionally substituted pyridines and 1,2,4-triazolo[1,5-a]pyridines. The obtained compounds carry latent functional substituents and are thus interesting for utility in further chemical transformations and for biological evaluation. Compounds **1b–d** were prepared by condensing malononitriles with the appropriate aryl methyl ketone in the presence of ammonium acetate and acetic acid under reflux in benzene solution, as has been reported earlier for preparation of **1c** [1].

Compounds **1a–c** reacted with triethyl orthoformate in refluxing acetic anhydride to yield the ethoxy derivatives **2a–c** in good yields. Although this condensation reaction may also afford the *cis* isomer of **2**, only the *trans* isomers **2** were formed, as $^1$H-NMR spectroscopy of the reaction products revealed, in

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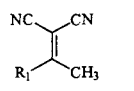
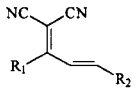
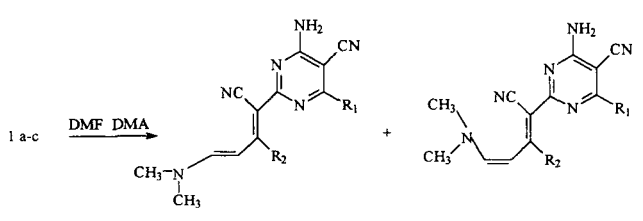
each case, two doublets at $\delta$ 6.50 and $\delta$ 6.90 for olefinic protons with $J$ = 13 Hz. This coupling constant value is typical for *trans* olefinic protons. Unexpectedly, trials to condense **1a–d** with triethyl orthoformate in N,N-dimethylformamide solution resulted in formation of N,N-dimethylaminodienes **2d–g**. Again, only *trans* isomers **2** were isolated, as olefinic protons appeared as two doublets at $\delta$ 5.90 and $\delta$ 6.70 with $J$ = 13 Hz, the typical value for *trans* olefinic protons. Compound **2g** proved to be identical with the product previously obtained from reaction of **1c** with N,N-dimethylformamide dimethylacetal (DMFDMA) in refluxing acetic acid [16]. In the same way, compounds **2d–f** were formed from the reactions of **1a,b,d** with DMFDMA. We first believed that formation of **2d–g** from reactions of **1a–d** with DMF in the presence of triethyl orthoformate is a result of condensations of DMF with **1a–d**. However, this proved to be incorrect, as compounds **1a–d** were recovered unaffected after long reflux in DMF. We thus believe that DMF first reacts with triethyl orthoformate to generate DMFDMA *in situ* which condenses with the active methyl moiety in **1a–d** to yield **2d–g**. To our knowledge, this is the first reported use of triethyl orthoformate in DMF as a synthetic equivalent for DMFDMA. In a trial to effect condensations of **1a–c** with DMFDMA in refluxing p-xylene, compounds **2e–g** were formed only as minor products. The major product in each case was a mixture of the *cis* and *trans* aminopyridine derivatives **3** and **4** or only one of these. Pure samples of **3b** as well as **4b** could be obtained by extracting the reaction mixture with ethyl acetate and evaporation of the extract. The mixture of **3a** and **4a** could not be separated. A similar reaction of **1c** with DMFDMA gave a mixture of **2g** and **3c**.



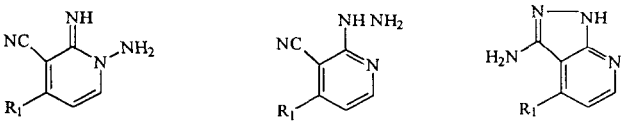
**1** a, $R_1$ = 2- Naphthyl
b, $R_1$ = 2- Thienyl
c, $R_1$ = 2- Phenyl
d, $R_1$ = 2- Furyl



**2** a, $R_1$ = 2- Naphthyl; $R_2$ = $OC_2H_5$
b, $R_1$ = 2- Thienyl; $R_2$ = $OC_2H_5$
c, $R_1$ = Phenyl; $R_2$ = $OC_2H_5$
d, $R_1$ = 2- Furyl; $R_2$ = $N(CH_3)_2$
e, $R_1$ = 2-Naphthyl; $R_2$ = $N(CH_3)_2$
f, $R_1$ = 2-Thienyl; $R_2$ = $N(CH_3)_2$
g, $R_1$ = Phenyl; $R_2$ = $N(CH_3)_2$

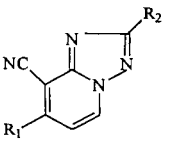


**3** **4**

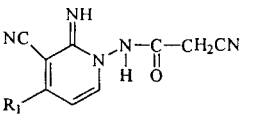


**5** **6** **7**

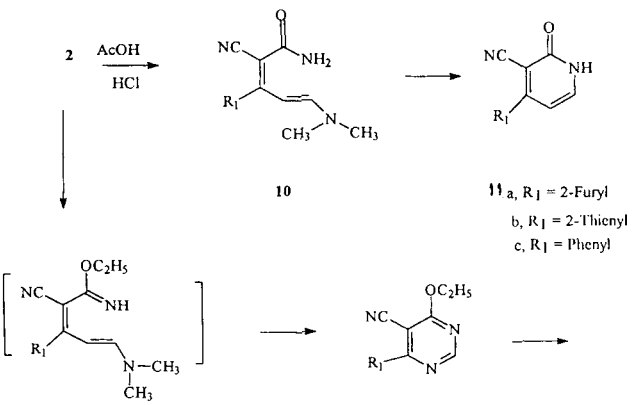
**3-7** a, $R_1$ = 2-Naphthyl
b, $R_1$ = 2-Thienyl
c, $R_1$ = Phenyl



**8a**, $R_1$ = 2-Naphthyl; R = Ph
b, $R_1$ = 2-Thienyl; R = Ph
c, $R_1$ = 2-Naphthyl; $R_2$ = H
d, $R_1$ = 2-Thienyl; $R_2$ = H



**9** a, $R_1$ = 2-Naphthyl
b, $R_1$ = Phenyl

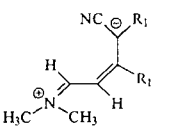


**10**

**11** a, $R_1$ = 2-Furyl
b, $R_1$ = 2-Thienyl
c, $R_1$ = Phenyl

**12**

**13** a, $R_1$ = 2-Furyl
b, $R_1$ = Phenyl



**14**

Compounds **2a,b** reacted with hydrazine hydrate to yield products of addition and ethanol elimination. These may be formulated as the N-aminopyridines **5a,b**, the hydrazinopyridines **6a,b**, or the pyrazolo[3,4-b]pyridines **7a,b**. The latter possibility was ruled out based on IR spectra which revealed, in each case, the presence of a cyano band in the products of the reaction of **2a,b** with hydrazine hydrate. The N-aminopyridine structure **5** was established for the reaction products based on their stability on reflux in acetic acid; under such conditions, compounds **6** are expected to cyclize readily into **7**. Moreover, the reaction products behaved typically as 1-amino-2-iminopyridines. Thus, with benzoyl chlo-

ride, compounds **5a,b** afforded the 1,2,4-triazolo[1,5-a]pyridines **8a,b**. Also **5a,b** reacted with DMFDMA to yield **8c,d**. Similar cyclizations of 1-amino-2-iminopyridines into 1,2,4-triazolo[1,5-a] pyridines have been reported in the patent literature [17,18]. Compounds **5a,b** were also formed from the reaction of **2e,f** with hydrazine hydrate. In contrast, **2c** reacted with hydrazine hydrate to yield only the pyrazolo[3,4-b]pyridineamine **7c**. The structure of this product is inferred from analytical and spectral data. Thus, the IR spectrum of the reaction product revealed the absence of a cyano band and the presence of an $NH_2$ group.

Compounds **5a,b** reacted with benzoyl chloride to yield **8a,b**. Also, the reactions of **5a,b** with DMFDMA gave **8c,d**.

Compounds **2a,c** or **2e,g** also reacted with cyanoethanoic hydride to yield the N-(cyanoacetamido)pyridines **9a,b**. The structure of **9** was established on the basis of spectral data (IR, $^1$H NMR, and $^{13}$C NMR). The IR spectrum showed C≡N absorption. The $^1$H NMR spectrum of **9** exhibited a signal of $\delta$ 4.2 for $CH_2$ and revealed H–6 as a doublet at $\delta$ 9.30 ($J$ = 9 Hz). $^{13}$C NMR spectra of the compound **9b** revealed signals for two C≡N groups as well as signals at $\delta$ 17.84 for the $CH_2$ group.

Compounds **2d,f,g** afforded the pyridones **11a–c** on treatment with acetic acid in the presence of aqueous hydrochloric acid. These products are thus assumed to be formed by initial hydrolysis of **2d,f,g** into the amides **10a–c** that readily cyclize into **11** by dimethylamine elimination. Compounds **11b,c** were also obtained from reactions of **2b,c** with acetic acid in the presence of concentrated hydrochloric acid. We believe that **10a–c** are intermediates in these transformations.

Compounds **2d,g** reacted with ethanolic sodium ethoxide to yield the ethoxypyridines **13a,b** which are believed to be formed by intermediary **12**. The $^1$H NMR spectra of compounds **2d–f**, **3b**, **3c**, and **4b** showed that the two methyl groups on the dimethylamino moieties are magnetically nonequivalent. This can be rationalized by assuming the predominance of charge-separated forms **14**. Yields of compounds obtained in this work are given in Table 1.

**TABLE 1** Yields for Compounds Obtained in This Article

| *Compound No.* | *Yield %* | *Compound No.* | *Yield %* |
|---|---|---|---|
| **1a** | 90 | **5b** | 88 |
| **2a** | 66 | **7c** | 70 |
| **2b** | 60 | **8a** | 95 |
| **2c** | 62 | **8b** | 82 |
| **2d** | 79.8 | **8c** | 96 |
| **2e** | 90 | **8d** | 79 |
| **2f** | 83 | **9a** | 84 |
| **2g** | 76 | **9b** | 85 |
| **3a + 4a** | 30 | **11a** | 92 |
| **3b** | 36 | **11b** | 86 |
| **3c** | 28 | **11c** | 90 |
| **4b** | 36 | **13a** | 90 |
| **5a** | 80.7 | **13b** | 86 |

## *EXPERIMENTAL*

All melting points are uncorrected. IR spectra (KBr) were recorded on a Shimadzu IR-740 spectrometer. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AC-80 spectrometer with DMSO as solvent and $SiMe_4$ as an internal standard; chemical shifts are reported in $\delta$ units. Microanalyses were performed with the University of Kuwait general facility apparatus LECO CNHS-932. Compounds **1b–d** were prepared by methods reported in the literature [1,13].

*1-(2-Naphthyl)-ethylidenemalononitrile* (**1a**). A suspension of 2-acetylnaphthalene (0.01 mol) in benzene (30 mL), ammonium acetate (0.01 mol), and acetic acid (2 mL) was treated with malononitrile (0.01 mol). The reaction mixture was refluxed for 10 minutes with stirring, then left at room temperature overnight. The solid product thus formed was collected by filtration and crystallized from ethanol.

*1-Naphth-2-ylethylidenemalononitrile* (**1a**). This compound was obtained as light brown crystals (90%) mp 113°C; IR: 2210 cm$^{-1}$ (CN); $^1$H NMR (DMSO): $\delta$ 2.70 (s, 3H, $CH_3$) and 7.60–8.40 (m, 7H, Ar–H). Anal. calcd. for $C_{15}H_{10}N_2$ (218.25): C, 82.54; H, 4.62; N, 12.84. Found: C, 82.33; H, 4.60; N, 12.85.

### *General Procedure for the Preparation of 3-Aryl-2-cyano-5-ethoxy-2,4-pentadienonitriles* (**2a–c**)

A suspension of each of **1a–c** (0.01 mol) in acetic anhydride (15 mL) was treated with triethyl orthoformate (0.01 mol). The reaction mixture was refluxed for 3 hours, then poured into water. The oily product thus formed solidified after a few hours and was crystallized from ethanol.

*2-Cyano-5-ethoxy-3-naphth-2-yl-2,4-pentadienonitrile* (**2a**). This compound was obtained as brown crystals (66%) mp 90°C; IR: 2225 (C≡N) and 1220 cm$^{-1}$ (C–O); $^1$H NMR ($CDCl_3$): $\delta$ 1.40 (t, 3H, $CH_3$, $J_{Hz}$ 8), 3.90 (q, 2H, $OCH_2$, $J_{Hz}$ 8); 6.50 (d, 1H, H–4, $J_{Hz}$ 13), 6.90 (d, 1H, H–5, $J_{Hz}$ 13), and 7.30–8.10 (m, 7H, Ar–H). Anal. calcd. for $C_{18}H_{14}N_2O$ (274.32): C, 78.81; H, 5.14; N, 10.21. Found: C, 78.36; H, 5.15; N, 10.29.

*2-Cyano-5-ethoxy-3-thien-2-yl-2,4-pentadienonitrile* (**2b**). This compound was obtained as gray crystals (60%) mp 65°C; IR: 2210 cm$^{-1}$ (C≡N); $^1$H NMR (DMSO): $\delta$ 1.40 (t, 3H, $CH_3$, $J_{Hz}$ 8); 4.50 (q, 2H, $OCH_2$, $J_{Hz}$ 8), 7.20–7.40 (m, 1H, and thienyl H–4); 7.90 (m, 2H, H–5, and thienyl H–3) and 8.40 (d, 1H, thienyl H–5, $J_{Hz}$ 5). Anal. calcd. for $C_{12}H_{10}N_2O$ S

(230.22): C, 62.60; H, 4.38; N, 12.17. Found: C, 62.64; H, 4.40; N, 12.22.

*2-Cyano-5-ethoxy-3-phenyl-2,4-pentadienonitrile* (**2c**). This compound was obtained as silvery crystals (62%); mp 87°C; IR: 2225 (C≡N), 1625 (C=C), and 1240 $cm^{-1}$ (C–O); $^1H$ NMR ($CDCl_3$): $\delta$ 1.30 (t, 3H, $CH_3$, $J_{Hz}$ 8); 4.60 (q, 2H, $OCH_2$, $J_{Hz}$ 8), 6.40 (d, 1H, H–4, $J_{Hz}$ 13), 6.90 (d, 1H, H–5, $J_{Hz}$ 13), and 7.30–7.60 (m, 5H, Ar–H). Anal. calcd. for $C_{14}H_{12}N_2O$ (224.25): C, 74.99; H, 5.38; N, 12.49. Found: C, 75.10; H, 5.52; N, 12.50.

## *General Procedure for the Preparation of 3-Aryl-2-cyano-5-(N,N-dimethylamino)-2,4-pentadienonitriles* (2d–g)

*Method (A).* A suspension of each of **1a–d** (0.01 mol) was treated with N,N-dimethylformamide (15 mL) and triethyl orthoformate (15 mL). The reaction mixture was refluxed for 4 hours, then poured into water. The oily product thus formed solidified after a few hours. This was filtered off and crystallized from ethanol.

*Method (B).* A suspension of each of **1a–d** (0.01 mol) in 30 mL of dioxane was treated with dimethylformamide dimethylacetal (0.01 mol). The reaction mixture was refluxed for 1 hour. The solid products thus formed were collected by filtration and crystallized from ethanol.

*2-Cyano-5-(N,N-dimethylamino)-3-fur-2-yl-2,4-pentadienonitrile* (**2d**). This compound was obtained in 79.8% yield as green crystals from ethanol, mp 155°C; ir: 2220 $cm^{-1}$ (C≡N); $^1H$ nmr ($CDCl_3$) $\delta$ 3.03 (s, 3H, $NCH_3$), 3.19 (s, 3H, $NCH_3$), 5.60 (d, 1H, H–4, $J_{Hz}$ 13), 6.60 (m, 1H, furyl H–4), 7.00 (m, 1H, furyl H-3), 7.40 (d, 1H, H–5, $J_{Hz}$ 13), and 7.70 (m, 1H, furyl H–5). Anal. calcd. for $C_{12}H_{11}N_3O$ (213.23): C, 67.59; H, 5.20; N, 19.71. Found: C, 67.21; H, 5.34; N, 19.52.

*2-Cyano-5-(N,N-dimethylamino)-3-naphth-2-yl-2,4-pentadienonitrile* (**2e**). This compound was obtained as violet green crystals (90%) mp 180°C; ir: 2220 (C≡N) $cm^{-1}$; $^1H$ nmr: ($CDCl_3$): 2.80 (s, 3H, $NCH_3$); 2.90 (s, 3H, $NCH_3$); 5.90 (d, 1H, H–4, $J_{Hz}$ 12.5); 6.70 (d, 1H, $J_{Hz}$ 12.5) and 7.20–8.00 (m, 7H, Ar–H). Anal. calcd. for $C_{18}H_{15}N_3$ (273.33): C, 79.09; H, 5.53; N, 15.37. Found: C, 79.30; H, 5.48; N, 15.41.

*2-Cyano-5-(N,N-dimethylamino)-3-thien-2-yl-pentadienonitrile* (**2f**). This compound was obtained as green crystals (83%) mp 160°C; ir: 2220 (C≡N) $cm^{-1}$. $^1H$ nmr ($CDCl_3$): $\delta$ 3.00 (S, 3H, $NCH_3$); 3.10 (s, 3H, $NCH_3$); 5.80 (d, 1H, H–4, $J_{Hz}$ 13) and 7.06–7.60 (m, 4H, H–5, and thienyl H). Anal. calcd. for $C_{12}H_{11}N_3S$ (229.30): C, 62.85; H, 4.83; N, 18.32; S, 13.96. Found: C, 62.58; H, 4.80; N, 18.33; S, 13.67.

*2-Cyano-5-(N,N-dimethylamino)-3-phenyl-2,4-pentadienonitrile* (**2g**). This compound was obtained in 76% yield as violet crystals (ethanol) mp 149°C; ir: 2220 (C≡N) $cm^{-1}$; $^1H$ nmr ($CDCl_3$) $\delta$ 3.00 [s, 6H, $N(CH_3)_2$], 5.80 (d, 1H, H–4, $J_{Hz}$ 13), 6.60 (d, 1H, H–5, $J_{Hz}$ 13), and 7.20–7.50 (m, 5H, Ar–H). Anal. calcd. for $C_{14}H_{13}N_3$ (223.27): C, 75.31; H, 5.87; N, 18.82. Found: C, 75.11; H, 5.99; N, 18.67.

## *General Procedure for the Preparation of 3-Aryl-5-dimethylamino-2-(2-amino-4-aryl-3-cyanopyrid-6-yl)-2,4-pentadienonitriles* (3a–c) *and* (4a–c)

To a solution of each of **1a–c** (0.01 mol) in 10 mL of *p*-xylene, (0.01 mol) of dimethylformamide, dimethylacetal was added. The reaction mixture was refluxed for 20 minutes, then evaporated in vacuo. The solid product obtained was a mixture of **2,3** and **4**. The reaction product was boiled with ethanol (50 mL) for 10 minutes and then filtered while hot. The remaining solid was a mixture of **3,4** in 60% yield. Evaporation of ethanol gave **2** in 30% yield. As for **3b** and **4b**, they were separated from each other by extraction with ethyl acetate, while the remaining solid product (36%) proved to be **4b**. Evaporation of the ethyl acetate gave **3b**. The mixture of **3a** and **4a** could not be separated.

*5-Dimethylamino-3-naphth-2-yl-2-(2-amino-3-cyano-4-naphth-2-ylpyrid-6-yl)-2,4-pentadienonitrile* (**3a** *and* **4a**) This mixture of compounds was obtained as light green crystals from ethyl acetate (30%) mp 184–187°C; ir: 3445, 3144 ($NH_2$), 2195 (C≡N), and 1610 $cm^{-1}$ (C=N); $^1H$ nmr (DMSO): $\delta$ 2.0 (br, 2H, $NH_2$); 3.0 [m, 12H, $2N(CH_3)_2$], 5.80 (m, 1H, H–4, $J_{Hz}$ 14); 6.30 (m, 1H, H–4), 6.90 (m, 1H, H–5, $J_{Hz}$ 14), 7.30–8.20 (m, 18H, Ar–H), and 8.60 (m, 1H, H–5). Anal. calcd. for $C_{33}H_{25}N_5$ (491.57): C, 80.63; H, 5.13; N, 14.25. Found: C, 80.51; H, 5.14; N, 14.25.

*(E,E)-5-Dimethylamino-3-thien-2-yl-2-(2-amino-3-cyano-4-thien-2-ylpyrid-6-yl)-2,4-pentadienonitrile* (**3b**) This was obtained as green crystals (36%) mp 67°C; ir: 3455–3300 ($NH_2$); 2150 (C≡N) and 1607 $cm^{-1}$ (C=N). $^1H$ nmr (DMSO): $\delta$ 1.85 (s, 2H, $NH_2$); 3.00 (s, 3H, $NCH_3$); 3.15 (s, 3H, $NCH_3$); 5.75 (d, 1H, H–4, $J_{Hz}$ 13); 7.00–7.90 (m, 8H, H–5, pyridyl H–5, and thienyl–H). Anal. calcd. for $C_{21}H_{17}N_5S_2$ (403.52): C, 62.52; H, 4.25; N, 17.36; S, 15.85. Found: C, 62.77; H, 4.54; N, 17.37; S, 15.53.

*(E,E)-5-Dimethylamino-3-phenyl-2-(2-amino-3-cyano-4-phenylpyrid-6-yl)-2,4-pentadienonitrile* (**3c**) This was obtained as yellow crystals (28%) mp 180°C; ir: 3430–3240 ($NH_2$) and 2190 $cm^{-1}$ (C≡N); $^1H$ nmr (DMSO): 1.80 (br, 2H, $NH_2$); 3.00 (s, 3H, $NCH_3$); 3.10 (s, 3H, $NCH_3$); 5.70 (d, 1H, H–4, $J_{Hz}$ 14), 6.90 (d, 1H, H–5, $J_{Hz}$ 14), and 7.20–7.60 (m, 1H, Ar–

H). Anal. calcd. for $C_{25}H_{21}N_5$ (391.46): C, 76.70, H, 5.41; N, 17.89. Found: C, 76.73; H, 5.29; N, 17.94.

*(E,Z)-5-Dimethylamino-3-thien-2-yl-2-(2-amino-3-cyano-4-thien-2-ylpyrid-6-yl)-2,4-pentadienonitrile* (**4b**). This was obtained as green crystals (36%) mp 185°C; ir: 3440, 3105 ($NH_2$), 2195 (C≡N), and 1623 $cm^{-1}$ (C=N); $^1H$ nmr (DMSO): $\delta$ 1.90 (s, 2H, $NH_2$); 3.10 (s, 3H, $NCH_3$); 3.30 (s, 3H, $NCH_3$); 6.10 (s, 1H, H–4); 7.00–7.70 (m, 7H, thienyl–H, and pyridyl H–5) and 8.50 (s, 1H, H–5). Anal. calcd. for $C_{21}H_{17}N_5S_2$ (403.52): C, 62.50; H, 4.24; N, 17.35; S, 15.89. Found: C, 62.66; H, 4.35; N, 17.34; S, 16.32.

### *General Procedure for the Preparation of 1-Amino-4-aryl-2-iminopyridine-3-carbonitriles* (5a,b) *and* 7c

To a solution of each of **2a–c** (0.01 mol) in 10 mL of ethanol, a few drops of hydrazine hydrate was added. The reaction mixture was refluxed for 30 minutes. The solid product thus formed was collected by filtration and crystallized from ethanol.

*1-Amino-2-imino-4-naphth-2-ylpyridine-3-carbonitrile* (**5a**). This compound was obtained as light green crystals from ethanol (80.7%) mp 210°C; ir: 3450 (NH), 3200–3300 ($NH_2$), 2220 (C≡N), and 1660 $cm^{-1}$ (C=N); $^1H$ nmr (DMSO): $\delta$ 3.30 (br, 2H, $NH_2$), 5.95 (d, 1H, pyridyl H–5, $J_{Hz}$ 6), and 6.5–8.3 (m, 9H, Ar–H, pyridyl H–6, and NH). Anal. calcd. for $C_{16}H_{12}N_4$ (260.29): C, 73.83; H, 4.65; N, 21.53. Found: C, 73.35; H, 4.95; N, 21.41.

*1-Amino-2-imino-4-thien-2-ylpyridine-3-carbonitrile* (**5b**). This compound was obtained as light green crystals from ethanol (88%) mp 212°C; ir: 3450 (NH); 3300 ($NH_2$), 2220 (C≡N), and 1640 $cm^{-1}$ (C=N); $^1H$ nmr (DMSO): $\delta$ 3.30 (br, 2H, $NH_2$), 6.10 (d, 1H, pyridyl H–5, $J_{Hz}$ 6), and 6.50 (br, 1H, NH); 7.30 (m, 1H, thienyl H–4); 7.40 (m, 3H, pyridyl H–6, and thienyl H–3, H–5). Anal. calcd. for $C_{10}H_8N_4S$ (216.27): C, 55.53; H, 3.72; N, 25.90; S, 14.82. Found: C, 55.42; H, 3.85; N, 25.90; S, 14.58.

*4-Phenylpyrazolo[3,4-b]pyridine-3-amine* (**7c**). This compound was obtained as pink crystals from ethanol (70%) mp 168°C; ir: 3435–3300 (NH and $NH_2$) and 1615 $cm^{-1}$ ($SNH_2$); $^1H$ nmr (DMSO): $\delta$ 4.50 (s, 1H, NH); 7.50–7.80 (m, 6H, Ar–H, and pyridyl H–5) and 9.30 (d, 1H, pyridyl H–6, $J_{Hz}$ 8). Anal. calcd. for $C_{12}H_{10}N_4$ (210.23): C, 68.55; H, 4.79; N, 26.65. Found: C, 68.66; H, 4.77; N, 26.66.

### *General Procedure for the Preparation of 7-Aryl-2-phenyl-1,2,4-triazolo[1,5-a]pyridine-8-carbonitrile* (8a–b)

An equimolar amount of each of **5a,b** (0.01 mol) and benzoyl chloride (0.01 mol) was dissolved in 10 mL of pyridine. The reaction mixture was then refluxed for 3 hours, then poured into water. The solid product thus formed was recrystallized from ethanol.

*7-Naphth-2-yl-2-phenyl-1,2,4-triazolo[1,5-a]pyridine-8-carbonitrile* (**8a**). This compound was obtained in 95% yield as yellow crystals (ethanol) mp 252°C; ir: 2225 (C≡N); and 1610 $cm^{-1}$ (C=N); $^1H$ nmr (DMSO); $\delta$ 7.40–8.50 (m, 13H, Ar–H, pyridyl H–6) and 9.30 (d, 1H, pyridyl H–5, $J_{Hz}$ 6). Anal. calcd. for $C_{23}H_{14}N_4$ (346.37): C, 79.75; H, 4.07; N, 16.18. Found: C, 79.39; H, 4.25; N, 16.07.

*2-Phenyl-7-thien-2-yl-1,2,4-triazolo[1,5-a]pyridine-8-carbonitrile* (**8b**). This compound was obtained in 82% yield as brown crystals (ethanol) mp 239°C; ir: 2225 (C≡N); and 1610 $cm^{-1}$ (C=N); $^1H$ nmr ($CDCl_3$): $\delta$ 7.30 (m, 5H, Ar–H); 7.50 (m, 1H, thienyl H–4); 7.70 (m, 1H, thienyl H–3); 8.60–8.30 (m, 2H, pyridyl H–6, and thienyl H–5) and 8.90 (d, 1H, pyridyl H–5, $J_{Hz}$ 6). Anal. calcd. for $C_{17}H_{10}N_4S$ (302.28): C, 67.55; H, 3.31; N, 18.53; S, 10.60. Found: C, 67.45; H, 3.49; N, 18.49; S, 10.38.

### *General Procedure for the Preparation of 7-Aryl-1,2,4-triazolo[1,5-a]pyridine-8-carbonitrile* (8c–d)

Equimolar amounts of each of **5a,b** (0.01 mol) and dimethylformamide dimethylacetal (0.01 mol) were dissolved in 10 mL of dioxane. The reaction mixture was refluxed for 2 hours, then poured into water. The solid product thus formed was recrystallized from ethanol.

*7-Naphth-2-yl-1,2,4-triazolo[1,5-a]pyridine-8-carbonitrile* (**8c**). This compound was obtained as light brown crystals (96%) mp 202°C; ir: 2225 (C≡N) and 1610 $cm^{-1}$ (C=N); $^1H$ nmr ($CDCl_3$); $\delta$ 7.30 (d, 1H, pyridyl H–6, $J_{Hz}$ 7); 7.50–8.30 (m, 7H, Ar–H); 8.50 (s, 1H, triazolyl H–2) and 8.90 (d, 1H, pyridyl H–5, $J_{Hz}$ 7). Anal. calcd. for $C_{17}H_{10}N_4$ (270.28): C, 75.54; H, 3.73; N, 20.73. Found: C, 75.52; H, 4.06; N, 20.56.

*7-Thien-2-yl-1,2,4-triazolo[1,5-a]pyridine-8-carbonitrile* (**8d**). This compound was obtained as light brown crystals (79%) mp 253°C; ir: 2225 $cm^{-1}$ (C≡N); $^1H$ nmr ($CDCl_3$); $\delta$ 7.20–7.40 (m, 2H, pyridyl H–6, and thienyl H–4); 7.70 (m, 2H, thienyl H–3, and H–5) and 8.00 (m, 2H, triazolyl H–2, and pyridyl H–5). Anal. calcd. for $C_{11}H_6N_4S$ (226.25): C, 58.39; H, 2.67; N, 24.76, S, 14.17. Found: C, 58.05; H, 2.75; N, 24.68; S, 13.70.

### *General Procedure for the Preparation of 4-Aryl-2-imino-N-(cyanoacetamido)-pyridine-3-carbonitrile* (9a,b)

In a 100 mL flask, a suspension of each of **2a,c** or **2e,g** (0.01 mol) in DMF (30 mL) was treated with

cyanoethanoic hydride (0.01 mol). The reaction mixture was refluxed for 3 hours, then poured into water. The solid product thus formed was collected by filtration and crystallized from ethanol.

*2-Imino-4-naphth-2-yl-N-(cyanoacetamido)pyridine-3-carbonitrile* (**9a**). This compound was obtained as red crystals from ethanol (84%); mp 179°C; ir: 3430–3220 (NH); 2175 (C≡N) and 1612 $cm^{-1}$ (amide CO); $^1H$ nmr (DMSO): $\delta$ 4.50 (s, 2H, $CH_2$); 7.20–7.90 (m, 11H, Ar–H, pyridyl H–5, and 2NH) and 9.30 (d, 1H, H–6, $J_{Hz}$ 9). Anal. calcd. for $C_{19}H_{13}N_5O$ (327.34): C, 69.71; H, 4.00. Found: C, 69.60; H, 4.44.

*2-Imino-4-phenyl-N-(cyanoacetamido)pyridine-3-carbonitrile* (**9b**). This compound was obtained as red crystals from ethanol (85%); mp 168°C; ir: 3415–3220 (NH); 2220 (C≡N) and 1611 $cm^{-1}$ (amide CO); $^1H$ NMR (DMSO): $\delta$ 4.50 (s, 2H, $CH_2$); 7.30–7.80 (m, 9H, Ar–H, pyridyl H–5, and 2NH) and 9.30 (d, 1H, H–6, $J_{Hz}$ 9). $^{13}C$ NMR (DMSO): $\delta$ 159.51 (C=O); 150.62 (C–2), 149.89 (C–6), 135.21 (C–4); 130.31 (C–5), 132.84, 128.97, 128.75, 126.38 (phenylcarbons), 116.48 (C≡N), 115.66 (C≡N), 114.9 (C–3), and 17.84 ($CH_2$). Anal. calcd. for $C_{15}H_{11}N_5O$ (277.28): C, 64.97; H, 4.00, N, 25.26. Found: C, 64.97; H, 3.90; N, 25.18.

## *General Procedure for the Preparation of 4-Aryl-3-oxo-pyridine-3-carbonitriles* (11a–c)

A solution of each of **2b,c** or **2d,f,g** (0.01 mol) in acetic acid hydrochloric acid (2:1) mixture (30 mL) was refluxed for 2 hours, then poured into water. The solid product thus formed was collected by filtration and crystallized from ethanol.

*4-Fur-2-yl-2-oxopyridine-3-carbonitrile* (**11a**). This compound was obtained as light brown crystals from ethanol (92%) mp 314°C; ir: 3450–3300 (NH), 2225 (C≡N), and 1650 $cm^{-1}$ (amide CO); $^1H$ NMR (DMF): $\delta$ 6.80 (m, 2H, pyridyl H–5, and furyl H–4), 7.70–7.90 (m, 3H, H–6, and furyl H–3, H–5), and 12.30 (br, 1H, NH). Anal. calcd. for $C_{10}H_6N_2O_2$ (186.16): C, 64.51; H, 3.25; N, 15.05. Found: C, 64.83; H, 3.23; N, 15.20.

*2-Oxo-4-thien-2-ylpyridine-3-carbonitrile* (**11b**). This compound was obtained as light brown crystals (86%) mp 288°C; ir: 3295 (NH); 2220 (C≡N) and 1650 $cm^{-1}$ (amide CO); $^1H$ NMR (DMSO): $\delta$ 3.30 (br, 1H, NH), 6.50 (d, 1H, pyridyl H–5, $J_{Hz}$ 6); 7.30 (m, 1H, thienyl H–4); 7.70 (d, 1H, pyridyl H–6, $J_{Hz}$ 6) and 7.95 (m, 2H, thienyl H–3, and H–5). Anal. calcd. for $C_{10}H_6N_2SO$ (202.16): C, 59.39; H, 2.99; N, 13.85. Found: C, 59.40; H, 3.20; N, 13.95.

*2-Oxo-4-phenylpyridine-3-carbonitrile* (**11c**). This compound was obtained as white crystals (90%) mp 158°C; ir: 3450 (NH); 2220 (C≡N) and 1660 $cm^{-1}$ (amide CO); $^1H$ NMR (DMSO): $\delta$ 3.30 (br, 1H, NH), 6.40 (d, 1H, pyridyl H–5, $J_{Hz}$ 6); 7.55 (m, 5H, Ar–H) and 7.80 (d, 1H, pyridyl H–6, $J_{Hz}$ 6). Anal. calcd. for $C_{12}H_8N_2O$ (196.20): C, 73.46; H, 4.11; N, 14.28. Found: C, 73.61; H, 4.11; N, 14.12.

## *General Procedure for the Preparation of 3-Aryl-2-ethoxypyridine-3-Carbonitriles* (13a,b):

A solution of each **2d,g** (0.01 mol) in absolute ethanol (60 mL) was treated with sodium ethoxide (0.25 mol). The mixture was heated for 2 hours, then allowed to cool to room temperature and acidified with dil. HCl. The solid product thus formed was collected by filtration and crystallized from ethanol.

*2-Ethoxy-3-fur-2-ylpyridine-3-carbonitrile* (**13a**). This compound was obtained as light brown crystals from ethanol (90%) mp 108°C; ir: 2215 $cm^{-1}$ (C≡N); $^1H$ NMR (DMF): $\delta$ 1.30 (t, 3H, $CH_3$, $J_{Hz}$ 8), 4.50 (q, 2H, $OCH_2$, $J_{Hz}$ 8), 6.80 (m, 1H, furyl H–4), 7.40–8.10 (m, 3H, furyl H–3, H–5, and pyridyl H–5), and 8.40 (d, 1H, pyridyl H–6, $J_{Hz}$ 8.5). Anal. calcd. for $C_{12}H_{10}N_2O_2$ (214.22): C, 67.28; H, 4.71; N, 13.08. Found: C, 67.31; H, 4.82; N, 13.07.

*2-Ethoxy-3-phenylpyridine-3-carbonitrile* (**13b**). This compound was obtained as light brown crystals from ethanol (86%) mp 104°C; ir: 2215 $cm^{-1}$ (C≡N); $^1H$ NMR (DMSO): $\delta$ 1.40 (t, 3H, $CH_3$, $J_{Hz}$ 8), 4.50 (q, 2H, $OCH_2$, $J_{Hz}$ 8), 7.20–7.80 (m, 6H, Ar–H, and pyridyl H–5), and 8.50 (d, 1H, pyridyl H–6, $J_{Hz}$ 7). Anal. calcd. for $C_{14}H_{12}N_2O$ (224.25): C, 74.99; H, 5.39; N, 12.49. Found: C, 74.93; H, 5.47; N, 12.50.

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