An Expeditious Synthesis of Heteroarenes through Carbanion-Induced Ring Transformation Reactions of Suitable Functionalized Pyran-2-ones[+]

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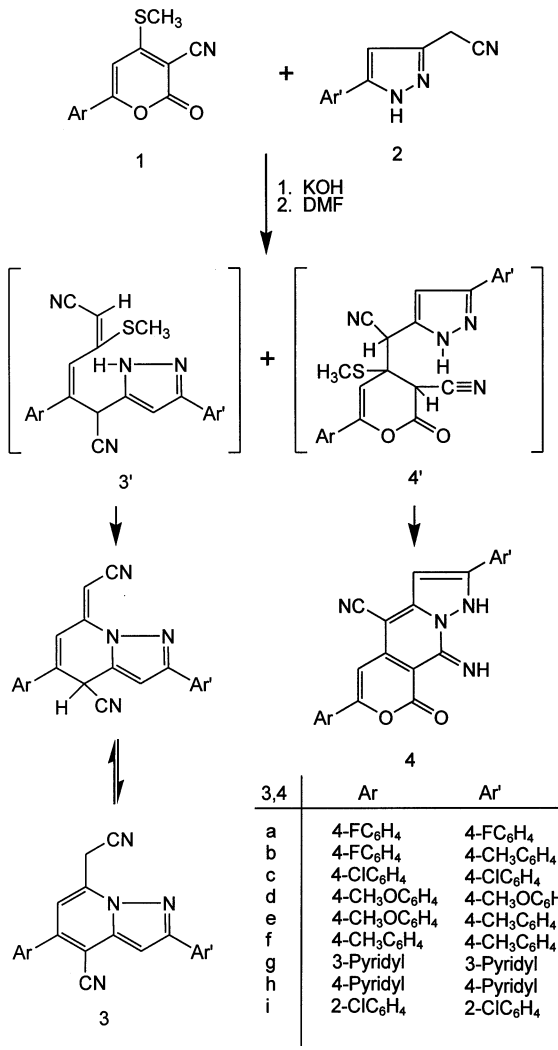
Pyrazolo[1,5-*a*]pyridines (**3**) and pyrano[4,3-*d*]pyrazolo[1,5-*a*]pyridines (**4**) have been synthesized from the reaction of pyran-2-one (**1**) and 5-aryl-3-cyanomethyl-1*H*-pyrazole (**2**) through carbanion-induced ring transformation reactions. A regioselective synthesis of highly functionalized polysubstituted pyrazolo[1,5-*a*]pyridines (**6**, **7**) has also been achieved from the reaction of **2** with polarised ketene dithioacetals (**5**) and arylidenemalononitrile, respectively. An analogous reaction of **1** with 2-cyanomethyl-1*H*-benzimidazole (**8**) has also afforded the fused heterocycles **9** and **10**. The cyano function in **9** has been exploited for acid-catalysed cyclization with thiosemicarbazide to obtain **11** in high yield.

Azolo[*a*]pyridines, being isosteric with purines, display diverse pharmacological activities, such as antihypertensive[1][2], antithrombotic[1], cardiotonic[1], antineoplastic[3] and anti-HIV activity,[3] depending upon the type and position of the substituents present in the molecular skeleton.

Heteroarenes such as pyrazolo[1,5-*a*]pyridines have been prepared previously either by the reaction of *N*-aminopyridinium salts[4] and acid chloride, or by the reaction of *N*-aminopyridinium ylides with dipolarophiles[5][6][7]. They have also been obtained in low yields by the thermal decarboxylation[8] of 2,6-diazatricyclo[5.2.1.0^{2,6}]deca-4,8-diene-3,10-diones. Alternatively, the oxidation of pyrazolinones in the presence of cyclopentadienone[8] also affords heteroarenes. Recently, a new synthesis of these compounds, by the reaction of 5-amino-4-cyano-3-cyanomethyl-1*H*-pyrazole with cinnamonitrile, has been reported[9]. However, under similar reaction conditions, an interaction between arylidenemalononitrile and 5-aryl-3-cyanomethyl-1*H*-pyrazole (**2**) failed to yield pyrazolo[1,5-*a*]pyridines. Instead 3-aryl-2-(5-aryl-1*H*-pyrazol-3-yl)acrylonitrile was isolated as a result of a retro Michael reaction, while heating in DMF in the presence of K_2CO_3 afforded polysubstituted pyrazolo[1,5-*a*]pyridine (**7**) with a yield of 21%.

Recently, pyrido[1,2-*a*]benzimidazoles have been prepared either by the ring transformation[10] reaction of pyrylium salts with 2-cyanomethyl-1*H*-benzimidazole (**8**), or by the cyclocondensation of **8** with 3-oxo esters[3]. These synthetic routes do not offer much scope for substituent variation and structural modification because of the limited choice of reagents used. Our synthetic strategy is based on the reaction of ambiphilic nucleophiles with the properly functionalized pyran-2-ones **1,** which have three different sets of 1,3-electrophilic centres in their molecular skeleton:

Scheme 1



3,4	Ar	Ar'
a	4-FC_6H_4	4-FC_6H_4
b	4-FC_6H_4	4-$CH_3C_6H_4$
c	4-ClC_6H_4	4-ClC_6H_4
d	4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$
e	4-$CH_3OC_6H_4$	4-$CH_3C_6H_4$
f	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$
g	3-Pyridyl	3-Pyridyl
h	4-Pyridyl	4-Pyridyl
i	2-ClC_6H_4	2-ClC_6H_4

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C^2-C^3-CN, $CN-C^3-C^4$ and $C^4-C^5-C^6$. Of the electrophilic centres, C^6 is highly susceptible to nucleophiles. Mobilization of any of the three sets of electrophilic centres in **1** by symmetrical or unsymmetrical ambiphilic nucleophiles resulted in a variety of nitrogen heterocycles, such as pyrazoles[11], isoxazoles[12], 2-aminopyridines[13], and 2-iminopyridines[14]. The synthetic utility of pyran-2-ones **1** as synthons was further explored using carbanions as nucleophiles for the synthesis of heteroarenes. A reaction of **1** and 1,3-C,N-ambident nucleophiles, such as 5-aryl-3-cyanomethyl-1*H*-pyrazoles **2** or 2-cyanomethyl-1*H*-benzimidazole (**8**), led to the formation of pyrazolo[1,5-*a*]pyridines **3** and pyrido[1,2-*a*]benzimidazoles **9** as the major products in yields of 50−70%, while pyrano[4,3-*d*]pyrazolo[1,5-*a*]pyridines **4** and pyrano[4,3-*d*]pyrido[1,2-*a*]benzimidazoles **10** were obtained as minor products in yields of 7−20%. Competitive reaction at two different sites and the difference in the degree of susceptibility towards nucleophiles resulted in the formation of two different products from the single reaction.

However, highly functionalized pyrazolo[1,5-*a*]pyridines **6** were obtained in high yields, and with a high degree of regioselectivity, by the reaction of **2** and the ketene dithioacetal (**5**).

Results and Discussion

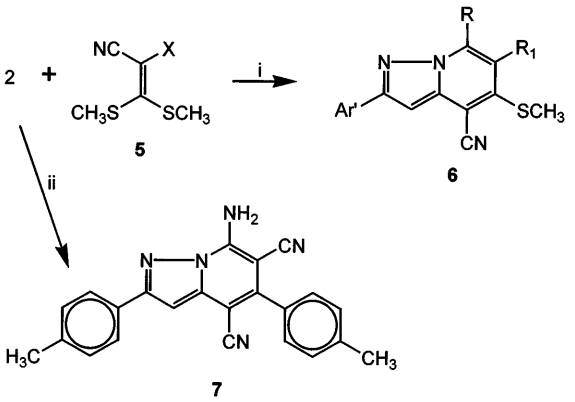
6-Aryl-3-cyano-4-methylthio-2*H*-pyran-2-ones **1** were synthesized[15] by base-catalyzed condensation-cyclization of aryl ketones with ethyl 2-cyano-3,3-dimethylthioacrylate. This paper reports an elegant route which gives easy access to the highly functionalized pyrazolo[1,5-*a*]pyridines **3** (the major product from the reaction of 5-aryl-3-cyanomethyl-1*H*-pyrazoles **2** and lactone **1)**. During the synthesis of **3**, a new minor product, pyrano[4,3-*d*]pyrazolo[1,5-*a*]pyridine (**4**), was also isolated and characterized (Scheme 1). In the case where there was a 2-substituted aryl substituent at position 6 of lactone **1**, this afforded **4** exclusively, possibly due to steric factors which force the reaction to adopt this pathway.

The ^{1}H-NMR spectrum of **3c** showed a characteristic singlet for methylene protons at δ = 4.45 and two singlets at δ = 7.15 and 7.18 due to 3-H and 6-H protons. Four doublets at δ = 7.46, 7.56, 7.64, and 7.96 were attributed to eight aromatic protons, which confirmed the structure of **3c**, while the structure of **4c** was confirmed due to presence of two D_2O exchangable NH protons with signals at δ = 7.46 and 9.24. Polysubstituted pyrazolo[1,5-*a*]pyridines (**6**, **7**) were also prepared from the reaction of 5-aryl-3-cyanomethyl-1*H*-pyrazole (**2**) with polarised ketene dithioacetals (**5**) and 2-cyano-3-(4-methylphenyl)acrylonitrile, respectively (Scheme 2).

An analogous reaction of **1** with 2-cyanomethyl-1*H*-benzimidazole (**8**) led to the formation of pyrido[1,2-*a*]benzimidazoles (**9**) and pyrano[4,3-*d*]pyrido[1,2-*a*]benzimidazoles (**10**) (Scheme 3).

The difference in degree of electrophilicity of positions C-6 and C-4 and their vulnerability to nucleophiles were the main reasons for the formation of a pair of products (**3**, **4** or **9**, **10**) from each reaction. The transformation of **1** to **3** was possibly initiated by nucleophilic attack at C-6 with ring opening followed by decarboxylation and a Michael addition with concomitant elimination of methanethiol,

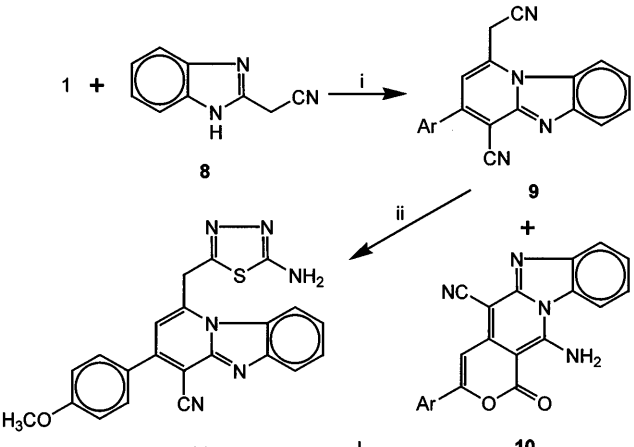
Scheme 2



6	Ar'	R	R_1
a	4-FC_6H_4	OH	CN
b	2-ClC_6H_4	OH	CN
c	4-ClC_6H_4	OH	CN
d	4-BrC_6H_4	OH	CN
e	4-$CH_3OC_6H_4$	OH	CN
f	3-Pyridyl	OH	CN
g	4-Pyridyl	OH	CN
h	2-ClC_6H_4	NH_2	CN
i	4-ClC_6H_4	NH_2	CN
j	4-$CH_3OC_6H_4$	NH_2	CN
k	3-Pyridyl	NH_2	CN
l	4-Pyridyl	NH_2	CN
m	4-ClC_6H_4	NH_2	4-ClC_6H_4
n	4-$CH_3OC_6H_4$	CH_3	$COCH_3$

(i) Dry DMF, K_2CO_3, 150°C; (ii) 4-$CH_3C_6H_4CH{=}C(CN)_2$, DMF, K_2CO_3, 150°C.

Scheme 3



9,10	Ar
a	4-FC_6H_4
b	4-ClC_6H_4
c	4-BrC_6H_4
d	4-$CH_3OC_6H_4$
e	4-$CH_3C_6H_4$

(i) Dry DMF, KOH, 30°C; (ii) $H_2NC(S)NHNH_2$, TFA, 70°C.

while the formation of **4** was as a result of competitive nucleophilic attack at C-4 followed by ring closure involving the cyano function. The formation of products **9** and **10** from the reaction of **1** and **8** also followed the same reaction course. A plausible mechanism for this transformation is depicted in Scheme 1.

The cyano function in the alkyl chain of **9** was also exploited for building the 1,3,4-thiadiazole moiety by acid-catalysed cyclisation with thiosemicarbazide to yield **11**.

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Experimental Section

General: Melting points: Büchi-530 melting point apparatus, open capillary, values uncorrected. − ^{1}H-NMR spectra: Perkin-Elmer (90 MHz), EM-360 (60 MHz), Bruker WM (300 MHz), and Bruker WM (400 MHz) NMR spectrometer using TMS as reference compound. − ^{13}C-NMR spectra : Bruker WM (400 MHz) spectrometer. − IR spectra: Perkin Elmer AC-1 spectrophotometer (KBr). − Electron-Impact mass spectra: Jeol JMS-D 300 spectrometer (70 eV). − Microanalyses: Carlo Erba EA-1108 elemental analyzer, within ± 0.5% of the theoretical values. − Thin layer chromatography (TLC): 7 × 3 cm precoated silica gel plastic plates.

Synthesis of 2,5-Diaryl-4-cyano-7-cyanomethylpyrazolo[1,5-a]pyridines **3** *and 6,10-Diaryl-8-cyano-3-imino-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridines* **4**. − *General Procedure:* A mixture of 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-one (**1**, 1 mmol) and 5-aryl-3-cyanomethyl-1*H*-pyrazole (**2**, 1 mmol) in dry DMF (12 ml) containing powdered KOH (0.056 g, 1 mmol) was stirred at ambient temp. for 2 d. After completion of the reaction, the mixture was poured into water whilst stirring and acidified with 10% HCl. The precipitate obtained was filtered to give a mixture of **3** and **4**. Both the compounds were separated on a silica gel column by using chloroform/hexane (1:1) as the eluent.

4-Cyano-7-cyanomethyl-2,5-bis(4-fluorophenyl)pyrazolo[1,5-a]pyridine (**3a**): Yield 48%; m.p. 275°C. − ^{1}H NMR ($CDCl_3$): δ = 4.46 (s, 2 H), 7.15 (s, 1 H), 7.18 (s, 1 H), 7.22 (t, 2 H), 7.29 (t, 2 H), 7.66−7.76 (m, 2 H), 7.96−8.06 (m, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN). − MS (70 eV); *m/z* (%): 370 [M^+] (100). − $C_{22}H_{12}F_2N_4$: calcd. C 71.34, H 3.27, N 15.13; found C 71.52, H 3.30, N 14.86.

4-Cyano-7-cyanomethyl-5-(4-fluorophenyl)-2-(4-methylphenyl)pyrazolo[1,5-a]pyridine (**3b**): Yield 52%; m.p. 225°C. − ^{1}H NMR ($CDCl_3$): δ = 2.42 (s, 3 H), 4.46 (s, 2 H), 7.12 (s, 1 H), 7.18 (s, 1 H), 7.22−7.34 (m, 4 H), 7.65−7.71 (m, 2 H), 7.90 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN). − MS (70 eV); *m/z* (%): 366 [M^+] (28.3). − $C_{23}H_{15}FN_4$: calcd. C 75.39, H 4.13, N 15.29; found C 74.98, H 4.25, N 15.49.

4-Cyano-7-cyanomethyl-2,5-bis(4-chlorophenyl)pyrazolo[1,5-a]pyridine (**3c**): Yield 64%; m.p. 212°C. − ^{1}H NMR ($CDCl_3$): δ = 4.45 (s, 2 H), 7.15 (s, 1 H), 7.18 (s, 1 H), 7.46 (d, 2 H), 7.56 (d, 2 H), 7.64 (d, 2 H), 7.96 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2210 cm^{-1} (CN). − MS (70 eV); *m/z* (%): 403 [M^+] (100), 334 (21.7). − $C_{22}H_{12}Cl_2N_4$: calcd. C 65.52, H 3.00, N 13.89; found C 65.19, H 3.29, N 14.03.

4-Cyano-7-cyanomethyl-2,5-bis(4-methoxyphenyl)pyrazolo[1,5-a]pyridine (**3d**): Yield 66%; m.p. 230−32°C. − ^{1}H NMR ($CDCl_3$): δ = 3.89 (s, 3 H), 3.92 (s, 3 H), 4.45 (s, 2 H), 7.04 (d, 2 H), 7.08 (s, 1 H), 7.14 (d, 2 H), 7.28 (s, 1 H), 7.68 (d, 2 H), 7.96 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 2910 (CH_2). − MS (70 eV); *m/z* (%): 394 [M^+] (100). − $C_{24}H_{18}N_4O_2$: calcd. C 73.01, H 4.24, N 13.1; found C 73.42, H 4.24, N 13.19.

4-Cyano-7-cyanomethyl-5-(4-methoxyphenyl)-2-(4-methylphenyl)pyrazolo[1,5-a]pyridine (**3e**): Yield 60%; m.p. 205°C. − ^{1}H NMR ($CDCl_3$): δ = 2.42 (s, 3 H), 3.90 (s, 3 H), 4.45 (s, 2 H), 7.08 (d, 2 H), 7.12 (s, 1 H), 7.15 (s, 1 H), 7.30 (d, 2 H), 7.68 (d, 2 H), 7.90 (d, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 20.60, 21.35, 55.47, 95.60, 111.50, 114.47, 114.72, 115.89, 126.67, 127.97, 128.99, 129.61, 130.01, 134, 139.61, 141.16, 143.79, 155.88, 161.27. − IR (KBr): $\tilde{\nu}$ = 2210 cm^{-1} (CN). − MS (70 eV); *m/z* (%): 378 [M^+] (100). − $C_{24}H_{18}N_4O$: calcd. C 76.17, H 4.79, N 14.81; found C 76.45, H 4.82, N 15.09.

4-Cyano-7-cyanomethyl-2,5-bis(4-methylphenyl)pyrazolo[1,5-a]pyridine (**3f**): Yield 61%; m.p. 186°C. − ^{1}H NMR ($CDCl_3$): δ = 2.43 (s, 3 H), 2.46 (s, 3 H), 4.44 (s, 2 H), 7.12 (s, 1 H), 7.14 (s, 1 H), 7.30 (d, 2 H), 7.38 (d, 2 H), 7.61 (d, 2 H), 7.90 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN). − MS (70 eV); *m/z* (%): 362 [M^+] (100). − $C_{24}H_{18}N_4$: calcd. C 79.53, H 5.01, N 15.46; found C 79.56, H 5.39, N 15.72.

4-Cyano-7-cyanomethyl-2,5-bis(3-pyridyl)pyrazolo[1,5-a]pyridine (**3g**): Yield 55%; m.p. > 265°C. − ^{1}H NMR ([D_6]DMSO): δ = 4.78 (s, 2 H), 7.42 (s, 1 H), 7.58 (t, 1 H), 7.66 (t, 1 H), 7.78 (s, 1 H), 8.22 (d, 1 H), 8.52 (d, 1 H), 8.68 (d, 1 H), 8.80 (d, 1 H), 8.98 (s, 1 H), 9.36 (s, 1 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 2900 (CH_2). − MS (70 eV); *m/z* (%): 336 [M^+] (61.6). − $C_{20}H_{12}N_6$: calcd. C 71.41, H 3.59, N 24.98; found C 70.91, H 3.43, N 24.65.

4-Cyano-7-cyanomethyl-2,5-bis(4-pyridyl)pyrazolo[1,5-a]pyridine (**3h**):Yield 52%; m.p. > 265°C. − ^{1}H NMR ([D_6]DMSO): δ = 5.28 (s, 2 H), 7.82 (s, 1 H), 8.20 (d, 2 H), 8.26 (s, 1 H), 8.54 (d, 2 H), 9.16 (d, 2 H), 9.26 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 2900 (CH_2). − MS (70 eV); *m/z* (%): 336 [M^+] (81.6). − $C_{20}H_{12}N_6$: calcd. C 71.41, H 3.59, N 24.98; found C 71.39, H 3.28, N 24.65.

8-Cyano-6,10-bis(4-fluorophenyl)-3-imino-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4a**): Yield 8%; m.p. 250°C. − ^{1}H NMR ($CDCl_3$): δ = 6.92 (s, 1 H), 7.06 (s, 1 H), 7.11−7.29 (m, 4 H), 7.50 (br. s, 1 H), 7.65−7.72 (m, 2 H), 7.90−8.02 (m, 2 H), 9.25 (br. s, 1 H). − IR (KBr): $\tilde{\nu}$ = 1700 cm^{-1} (CO), 2200 (CN), 3320 (NH). − MS (70 eV); *m/z* (%): 414 [M^+] (11), 398 (10.2). − $C_{23}H_{12}F_2N_4O_2$: calcd. C 66.66, H 2.92, N 13.52; found C 66.21, H 3.12, N 13.56.

8-Cyano-10-(4-fluorophenyl)-3-imino-6-(4-methylphenyl)-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4b**): Yield 12%; m.p. > 280°C. − ^{1}H NMR ($CDCl_3$): δ = 2.41 (s, 3 H), 6.92 (s, 1 H), 7.02 (s, 1 H), 7.2 (t, 2 H), 7.29 (t, 2 H), 7.50 (br. s, 1 H), 7.82−7.95 (m, 4 H), 9.22 (br. s, 1 H). − IR (KBr): $\tilde{\nu}$ = 1700 cm^{-1} (CO), 2190 (CN), 3320 (NH). − MS (70 eV); *m/z* (%): 410 [M^+] (100), 382 (11.6). − $C_{24}H_{15}FN_4O_2$: calcd. C 70.24, H 3.68, N 13.65; found C 70.50, H 3.61, N 13.94.

6,10-Bis(4-chlorophenyl)-8-cyano-3-imino-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4c**): Yield 14%; m.p. > 280°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 7.10 (s, 1 H), 7.29 (s, 1 H), 7.46 (br. s, 1 H), 7.55−7.65 (m, 4 H), 7.98 (d, 2 H), 8.19 (d, 2 H), 9.24 (br. s, 1 H). − IR (KBr): $\tilde{\nu}$ = 1710 cm^{-1} (CO), 2200 (CN), 3280 (NH). − MS (70 eV); *m/z* (%): 447 [M^+] (49.4). − $C_{23}H_{12}Cl_2N_4O_2$: calcd. C 61.76, H 2.71, N 12.53; found C 61.50, H 2.70, N 12.62.

8-Cyano-3-imino-6,10-bis(4-methoxyphenyl)-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4d**): Yield 7%; m.p. 250−52°C. − ^{1}H NMR ($CDCl_3$): δ = 3.83 (s, 3 H), 3.88 (s, 3 H), 6.82 (s, 1 H), 6.94 (s, 1 H), 6.96 (d, 2 H), 7.12 (d, 2 H), 7.45 (br. s, 1 H), 7.84 (d, 2

H), 7.91 (d, 2 H) 9.19 (br. s, 1 H). – IR (KBr): $\tilde{\nu}$ = 1710 cm^{-1} (CO), 2200 (CN), 3320 (NH). – MS (70 eV); *m/z* (%): 438 [M^+] (3.9). – $C_{25}H_{18}N_4O_4$: calcd. C 68.55, H 4.24, N 12.79; found C 68.31, H 4.28, N 12.36.

8-Cyano-3-imino-10-(4-methoxyphenyl)-6-(4-methylphenyl)-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4e**): Yield 15%; m.p. 278°C. – ^{1}H NMR ($CDCl_3$): δ = 2.44 (s, 3 H), 3.90 (s, 3 H), 6.92 (s, 1 H), 7.0 (d, 2 H), 7.04 (s, 1 H), 7.32 (d, 2 H), 7.50 (br. s, 1 H), 7.90 (dd, 4 H), 9.23 (br. s, 1 H). – IR (KBr): $\tilde{\nu}$ = 1680 cm^{-1} (CO), 2200 (CN), 3300 (NH). – MS (70 eV); *m/z* (%): 422 [M^+] (9.6). – $C_{25}H_{18}N_4O_3$: calcd. C 71.08, H 4.29, N 13.26; found C 70.89, H 4.35, N 13.25.

8-Cyano-3-imino-6,10-bis(4-methylphenyl)-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4f**): Yield 10%; m.p. > 280°C. – ^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 3 H), 2.44 (s, 3 H), 6.92 (s, 1 H), 7.08 (s, 1 H), 7.28–7.36 (dd, 4 H), 7.51 (br. s, 1 H), 7.82 (d, 2 H), 7.90 (d, 2 H), 9.25 (br. s, 1 H). – IR (KBr): $\tilde{\nu}$ = 1700 cm^{-1} (CO), 2200 (CN), 3320 (NH). – MS (70 eV); *m/z* (%): 406 [M^+] (100), 378 (8.8). – $C_{25}H_{18}N_4O_2$: calcd. C 73.88, H 4.46, N 13.79; found C 74.15, H 4.42, N 13.68.

8-Cyano-3-imino-6,10-bis(3-pyridyl)-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4g**): Yield 9%; m.p. > 260°C. – ^{1}H NMR ($CDCl_3$): δ = 7.24 (s, 1 H), 7.34 (s, 1 H), 7.44–7.48 (m, 1 H), 7.54–7.58 (m, 1 H), 8.06 (d, 1 H), 8.22 (br. s, 1 H), 8.32 (d, 1 H), 8.72 (d, 1 H), 8.84 (d, 1 H), 8.96 (s, 1 H), 9.20 (br. s, 1 H), 9.28 (s, 1 H). – IR (KBr): $\tilde{\nu}$ = 1700 cm^{-1} (CO), 2200 (CN), 3320 (NH). – MS (70 eV); *m/z* (%): 380 [M^+] (14.3). – $C_{21}H_{12}N_6O_2$: calcd. C 66.31, H 3.18, N 22.09; found C 66.52, H 3.52, N 22.31.

8-Cyano-3-imino-6,10-bis(4-pyridyl)-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4h**): Yield 10%; m.p. > 260°C. – ^{1}H NMR ($CDCl_3$): δ = 7.14 (s, 1 H), 7.32 (s, 1 H), 7.44 (br. s, 1 H), 7.62 (d, 2 H), 7.82 (d, 2 H), 7.92 (d, 2 H), 8.88 (d, 2 H), 9.46 (br. s, 1 H). – IR (KBr): $\tilde{\nu}$ = 1710 cm^{-1} (CO), 2200 (CN), 3320 (NH). – MS (70 eV); *m/z* (%): 380 [M^+] (1.8). – $C_{21}H_{12}N_6O_2$: calcd. C 66.31, H 3.18, N 22.09; found C 66.29, H 3.09, N 22.06.

6,10-Bis(2-chlorophenyl)-8-cyano-3-imino-2-oxopyrano[4,3-d]pyrazolo[1,5-a]pyridine (**4i**): Yield 44%; m.p. 250–52°C. – ^{1}H NMR ($CDCl_3$): δ = 7.18 (s, 1 H), 7.28 (s, 1 H), 7.40–7.48 (m, 5 H), 7.52–7.58 (m, 2 H), 7.72 (d, 1 H), 7.90–7.94 (m, 1 H), 9.30 (br. s, 1 H). – IR (KBr): $\tilde{\nu}$ = 1710 cm^{-1} (CO), 2200 (CN), 3250 (NH). – MS (70 eV); *m/z* (%): 446 [M^+] (100). – $C_{23}H_{12}Cl_2N_4O_2$: calcd. C 61.76, H 2.71, N 12.52; found C 61.30, H 2.92, N 12.10.

2-Aryl-4,6-dicyano-7-hydroxy-5-methylthiopyrazolo[1,5-a]pyridines **6a–g**. – *General Procedure:* A mixture of 5-aryl-3-cyanomethyl-1*H*-pyrazole (**2**, 10 mmol), ethyl 2-cyano-3,3-bis(methylthio)acrylate (2.17 g, 10 mmol), and K_2CO_3 (1.38 g, 10 mmol) in dry DMF (40 ml) was heated at 150°C for 2 h. The reaction mixture was then cooled, poured into water and the resulting solution acidified with 10% HCl. The crude solid obtained was filtered and crystallized from a suitable organic solvent.

4,6-Dicyano-2-(4-fluorophenyl)-7-hydroxy-5-methylthiopyrazolo-[1,5-a]pyridine (**6a**): Yield 56%; m.p. > 270°C. – ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 2.73 (s, 3 H), 6.8 (s, 1 H), 7.19 (t, 2 H), 7.94–8.14 (m, 2 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3540 (OH). – MS (70 eV); *m/z* (%): 324 [M^+] (34.5). – $C_{16}H_9FN_4OS$: calcd. C 59.25, H 2.80, N 17.28; found C 59.42, H 2.43, N 17.72.

2-(2-Chlorophenyl)-4,6-dicyano-7-hydroxy-5-methylthiopyrazolo[1,5-a]pyridine (**6b**): Yield 67%; m.p. 240–242°C. – ^{1}H NMR ([D_6]DMSO): δ = 2.64 (s, 3 H), 6.68 (s, 1 H), 7.45 (t, 2 H), 7.56–7.60 (m, 1 H), 7.86–7.90 (m, 1 H), 8.24 (s, 1 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3540 (OH). – MS (70 eV); *m/z* (%): 340 [M^+] (100). – $C_{16}H_9ClN_4OS$: calcd. C 56.38, H 2.66, N 16.44; found C 56.43, H 2.58, N 16.71.

2-(4-Chlorophenyl)-4,6-dicyano-7-hydroxy-5-methylthiopyrazolo[1,5-a]pyridine (**6c**): Yield 75%; m.p. > 270°C. – ^{1}H NMR ([D_6]acetone + [D_6]DMSO): δ = 2.70 (s, 3 H), 6.32 (s, 1 H), 7.01 (d, 2 H), 7.65 (d, 2 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3550 (OH). – MS (70 eV); *m/z* (%): 340 [M^+] (28.4), 294 (11.3). – $C_{16}H_9ClN_4OS$: calcd. C 56.39, H 2.66, N 16.44; found C 56.42, H 2.32, N 16.39.

2-(4-Bromophenyl)-4,6-dicyano-7-hydroxy-5-methylthiopyrazolo[1,5-a]pyridine (**6d**): Yield 60%; m.p. > 270°C. – ^{1}H NMR ($CDCl_3$ +[D_6]DMSO): δ = 2.76 (s, 3 H), 6.89 (s, 1 H), 7.64 (d, 2 H), 7.90 (d, 2 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3560 (OH). – MS (70 eV); *m/z* (%): 385 [M^+] (100). – $C_{16}H_9BrN_4OS$: calcd. C 49.88, H 2.35, N 14.54; found C 50.09, H 2.37, N 14.80.

4,6-Dicyano-7-hydroxy-2-(4-methoxyphenyl)-5-methylthiopyrazolo[1,5-a]pyridine (**6e**): Yield 74%; m.p. > 260°C. – ^{1}H NMR ([D_6]DMSO): δ = 2.64 (s, 3 H), 3.82 (s, 3 H), 6.76 (s, 1 H), 7.02 (d, 2 H), 7.94 (d, 2 H), 8.78 (br. s, 1 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3540 (OH). – MS (70 eV); *m/z* (%): 336 [M^+] (31.2). – $C_{17}H_{12}N_4O_2S$: calcd. C 60.70, H 3.59, N 16.65; found C 61.15, H 3.91, N 16.70.

4,6-Dicyano-7-hydroxy-5-methylthio-2-(3-pyridyl)pyrazolo[1,5-a]pyridine (**6f**): Yield 32%; m.p. > 265°C. – ^{1}H NMR ([D_6]DMSO): δ = 2.64 (s, 3 H), 7.02 (s, 1 H), 7.54–7.58 (m, 1 H), 8.52 (d, 2 H), 8.66 (s, 1 H), 9.62 (br. s, 1 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3550 (OH). – MS (70 eV); *m/z* (%): 307 [M^+] (41.9). – $C_{15}H_9N_5OS$: calcd. C 58.02, H 2.73, N 22.63; found C 58.41, H 2.95, N 22.79.

4,6-Dicyano-7-hydroxy-5-methylthio-2-(4-pyridyl)pyrazolo[1,5-a]pyridine (**6g**): Yield 48%; m.p. > 265°C. – ^{1}H NMR ([D_6]DMSO): δ = 2.64 (s, 3 H), 7.30 (s, 1 H), 8.56 (d, 2 H), 8.92 (d, 2 H), 9.20 (s, 1 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3550 (OH). – MS (70 eV); *m/z* (%): 307 [M^+] (20.8). – $C_{15}H_9N_5OS$: calcd. C 58.61, H 2.95, N 22.79; found C 58.82, H 2.82, N 22.81.

7-Amino-2-aryl-4,6-dicyano-5-methylthiopyrazolo[1,5-a]pyridines **6h–l**. – *General Procedure:* A mixture of 5-aryl-3-cyanomethyl-1*H*-pyrazole (**2**, 10 mmol) and 2-cyano-3,3-dimethylthioacrylonitrile (1.70 g, 10 mmol) in dry DMF (40 ml) containing K_2CO_3 (1.38 g, 10 mmol) was heated at 150°C. After 2 h, the reaction mixture was cooled, poured into water and acidified with 10% HCl. The precipitate was filtered, washed with water and crystallized from a suitable solvent.

7-Amino-2-(2-chlorophenyl)-4,6-dicyano-5-methylthiopyrazolo[1,5-a]pyridine (**6h**): Yield 44%; m.p. 185°C. – ^{1}H NMR ([D_6]DMSO): δ = 2.76 (s, 3 H), 7.12 (s, 1 H), 7.44 (t, 2 H), 7.54 (t, 1 H), 7.94 (t, 1 H), 8.32 (s, 2 H). – IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3320 (NH_2). – MS (70 eV); *m/z* (%): 339 [M^+] (41.1). – $C_{16}H_{10}ClN_5S$: calcd. C 56.55, H 2.96, N 20.61; found C 56.35, H 2.62, N 20.29.

7-Amino-2-(4-chlorophenyl)-4,6-dicyano-5-methylthiopyrazolo[1,5-a]pyridine (**6i**): Yield 62%; m.p. > 270°C. – ^{1}H NMR ([D_6]acetone): δ = 2.76 (s, 3 H), 7.16 (s, 1 H), 7.52 (d, 2 H), 8.16 (d, 2 H), 8.51 (br. s, 2 H). – IR (KBr): $\tilde{\nu}$ = 2220 cm^{-1} (CN), 3450 (NH_2). – MS (70 eV); *m/z* (%): 339 [M^+] (55.5), 293 (100), 111 (36). – $C_{16}H_{10}ClN_5S$: calcd. C 56.55, H 2.97, N 20.61; found C 56.36, H 3.25, N 20.50.

7-Amino-4,6-dicyano-2-(4-methoxyphenyl)-5-methylthiopyrazolo[1,5-a]pyridine (**6j**): Yield 47%; m.p. > 265°C. – ^{1}H NMR

([D_6]DMSO): δ = 2.74 (s, 3 H), 3.90 (s, 3 H), 6.86 (s, 1 H), 7.02 (d, 2 H), 7.94 (d, 2 H), 8.22 (s, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3420 (NH_2). − MS (70 eV); *m/z* (%): 335 [M^+] (54.8). − $C_{17}H_{13}N_5OS$: calcd. C 60.87, H 3.90, N 20.88; found C 60.97, H 4.13, N 21.03.

7-Amino-4,6-dicyano-5-methylthio-2-(3-pyridyl)pyrazolo[1,5-a]-pyridine (**6k**): Yield 49%; m.p. > 265°C. − ^{1}H NMR ([D_6]DMSO): δ = 2.74 (s, 3 H), 7.36 (s, 1 H), 7.56 (t, 1 H), 8.54 (d, 1 H), 8.64 (d, 1 H), 9.04 (s, 2 H), 9.36 (s, 1 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3420 (NH_2). − MS (70 eV); *m/z* (%): 306 [M^+] (33.1). − $C_{15}H_{10}N_6S$: calcd. C 58.73, H 3.18, N 27.40; found C 58.85, H 3.48, N 27.58.

7-Amino-4,6-dicyano-5-methylthio-2-(4-pyridyl)pyrazolo[1,5-a]-pyridine (**6l**): Yield 49%; m.p. > 265°C. − ^{1}H NMR ([D_6]DMSO): δ = 2.74 (s, 3 H), 7.46 (s, 1 H), 8.14 (d, 2 H), 8.74 (s, 2 H), 9.08 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3420 (NH_2). − MS (70 eV); *m/z* (%): 306 [M^+] (48.4). − $C_{15}H_{10}N_6S$: calcd. C 58.73, H 3.28, N 27.40; found C 58.35, H 3.56, N 27.11.

7-Amino-2,6-bis(4-chlorophenyl)-4-cyano-5-methylthio-pyrazolo[1,5-a]pyridine (**6m**): 2-(4-chlorophenyl)-3,3-dimethylthioacrylonitrile (0.26 g, 1 mmol) and K_2CO_3 (0.138 g, 1 mmol) were added to a solution of 5-(4-chlorophenyl)-3-cyanomethyl-1*H*-pyrazole (0.217 g, 1 mmol) in dry DMF (5 ml). The reaction mixture was heated at 150°C for 2 h. After completion of the reaction, it was cooled, poured into water and acidified with 10% HCl. The yellow precipitate obtained was filtered and the product purified on a silica gel column by using $CHCl_3$ as the eluent. Yield 84%; m.p. 190−92°C. − ^{1}H NMR ($CDCl_3$): δ = 2.36 (s, 3 H), 5.66 (br. s, 2 H), 6.92 (s, 1 H), 7.35 (d, 2 H), 7.45 (d, 2 H), 7.54 (d, 2 H), 7.92 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3360 (NH_2). − MS (70 eV); *m/z* (%): 425 [M^+] (14.5), 169 (100). − $C_{21}H_{14}Cl_2N_4S$: calcd. C 59.29, H 3.32, N 13.17; found C 58.96, H 3.42, N 12.87.

6-Carbomethyl-4-cyano-2-(4-methoxyphenyl)-7-methyl-5-methylthiopyrazolo[1,5-a]pyridine (**6n**): A mixture of 3-cyanomethyl-5-(4-methoxyphenyl)-1*H*-pyrazole (2.13 g, 10 mmol), 1-acetyl-2,2-bis-(methylthio)vinyl methyl ketone (2.04 g, 10 mmol) and K_2CO_3 (1.38 g, 10 mmol) in dry DMF (40 ml) was heated as described in the preceding experiment. The crude product was purified on a silica gel column by using chloroform/hexane (3:1) as the solvent, Yield 30%; m.p. 150°C. − ^{1}H NMR ($CDCl_3$): δ = 2.58 (s, 3 H), 2.66 (s, 3 H), 2.78 (s, 3 H), 3.86 (s, 3 H), 6.85 (s, 1 H), 6.98 (d, 2 H), 7.92 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 1690 cm^{-1} (CO), 2210 (CN), 2920 (CH_3). − MS (70 eV); *m/z* (%): 351 [M^+] (32.4), 336 (38.4), 309 (100). − $C_{19}H_{17}N_3O_2S$: calcd. C 64.93, H 4.88, N 11.96; found C 64.69, H 5.13, N 12.24.

7-Amino-4,6-dicyano-2,5-bis(4-methylphenyl)pyrazolo[1,5-a]-pyridine (**7**): The compound was synthesized from 3-cyanomethyl-5-(4-methylphenyl)-1*H*-pyrazole (0.197 g, 1 mmol) and 2-cyano-3-(4-methylphenyl)acrylonitrile (0.168 g, 1 mmol), as described in the preceding experiment, and the product was purified on a silica gel column using chloroform/hexane (10:1) as the solvent. Yield 21%; m.p. > 270°C. − ^{1}H NMR ($CDCl_3$): δ = 2.44 (s, 3 H), 2.46 (s, 3 H), 6.96 (s, 1 H), 7.30 (d, 2 H), 7.36 (d, 2 H), 7.48 (d, 2 H), 7.90 (d, 2 H). − IR (KBr): $\tilde{\nu}$ = 2200 cm^{-1} (CN), 3440 (NH_2). − MS (70 eV); *m/z* (%): 363 [M^+] (100), 348 (26.1). − $C_{23}H_{17}N_5$: calcd. C 76.01, H 4.72, N 19.27; found C 75.81, H 4.71, N 19.34.

General Procedure for the Synthesis of 3-Aryl-4-cyano-1-cyanomethylpyrido[1,2-a]benzimidazoles **9** *and 3-Amino-12-aryl-10-cyano-2-oxopyrano[4,3-d]pyrido[1,2-a]benzimidazoles* **10**: A mixture of 6-aryl-3-cyano-4-methylthio-2*H*-pyran-2-one (**1**, 10 mmol), 2-cyanomethyl-1*H*-benzimidazole (**8**, 10 mmol) and powdered KOH (0.56 g, 10 mmol) in dry DMF (40 ml) was stirred at room temp. for 2 d. The reaction mixture was poured into water and a precipitate was obtained after acidification with 10% HCl. This was then filtered to give a mixture of **9** and **10**, which were separated on a silica gel column by using chloroform/hexane (1:1) as the solvent.

4-Cyano-1-cyanomethyl-3-(4-fluorophenyl)pyrido[1,2-a]-benzimidazole (**9a**): Yield 51%; m.p. 255°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 4.94 (s, 2 H), 7.23 (s, 1 H), 7.32 (t, 2 H), 7.52 (t, 1 H), 7.66 (t, 1 H), 7.78−7.88 (m, 2 H), 8.08 (d, 1 H), 8.19 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 2220 cm^{-1} (CN), 2920 (CH_2). − MS (70 eV); *m/z* (%): 326 [M^+] (56), 282 (44.9). − $C_{20}H_{11}FN_4$: calcd. C 73.61, H 3.39, N 17.17; found C 73.65, H 3.42, N 17.20.

3-(4-Chlorophenyl)-4-cyano-1-cyanomethylpyrido[1,2-a]-benzimidazole (**9b**): Yield 66%; m.p. > 280°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 4.88 (s, 2 H), 7.22 (s, 1 H), 7.53 (t, 1 H), 7.59 (d, 2 H), 7.66 (t, 1 H), 7.75 (d, 2 H), 8.1 (d, 1 H), 8.14 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 2220 cm^{-1} (CN). − MS (70 eV); *m/z* (%): 342 [M^+] (100), 317 (16.7), 304 (29.1). − $C_{20}H_{11}ClN_4$: calcd. C 70.08, H 3.24, N 16.35; found C 70.31, H 3.23, N 15.56.

3-(4-Bromophenyl)-4-cyano-1-cyanomethylpyrido[1,2-a]-benzimidazole (**9c**): Yield 65%; m.p. 262°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 4.98 (s, 2 H), 7.24 (s, 1 H), 7.52 (t, 1 H), 7.62-7.71 (m, 3 H), 7.78 (d, 2 H), 8.06 (d, 1 H), 8.20 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 2220 cm^{-1} (CN), 2930 (CH_2). − MS (70 eV); *m/z* (%): 387 [M^+] (100), 306 (18.2), 280 (12.8), 184 (16.4). − $C_{20}H_{11}BrN_4$: calcd. C 62.03, H 2.86, N 14.47; found C 61.89, H 2.82, N 14.50.

4-Cyano-1-cyanomethyl-3-(4-methoxyphenyl)pyrido[1,2-a]-benzimidazole (**9d**): Yield 69%; m.p. 267°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 3.95 (s, 3 H), 4.85 (s, 2 H), 7.12 (d, 2 H), 7.25 (s, 1 H), 7.52 (t, 1 H), 7.66 (t, 1 H), 7.79 (d, 2 H), 8.12 (dd, 2 H). − IR (KBr): $\tilde{\nu}$ = 2210 cm^{-1} (CN), 2920 (CH_2). − MS (70 eV); *m/z* (%): 338 [M^+] (22.3). − $C_{21}H_{14}N_4O$: calcd. C 74.54, H 4.17, N 16.56; found C 74.32, H 4.19, N 16.61.

4-Cyano-1-cyanomethyl-3-(4-methylphenyl)pyrido[1,2-a]-benzimidazole (**9e**): Yield 52%; m.p. 266°C. − ^{1}H NMR ($CDCl_3$): δ = 2.46 (s, 3 H), 4.62 (s, 2 H), 7.21 (s, 1 H), 7.41 (d, 2 H), 7.49 (t, 1 H), 7.65 (t, 1 H), 7.70 (d, 2 H), 7.94 (d, 1 H), 8.14 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 2220 cm^{-1} (CN), 2930 (CH_2). − MS (70 eV); *m/z* (%): 322 [M^+] (100). − $C_{21}H_{14}N_4$: calcd. C 78.24, H 4.38, N 17.38; found C 77.91, H 3.98, N 17.40.

3-Amino-10-cyano-12-(4-fluorophenyl)-2-oxopyrano[4,3-d]-pyrido[1,2-a]benzimidazole (**10a**): Yield 18%; m.p. > 270°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 7.13 (s, 1 H),7.25 (t, 2 H), 7.31 (t, 1 H), 7.51 (t, 1 H), 7.73−7.78 (m, 2 H), 7.92 (d, 1 H), 8.46 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 1700 cm^{-1} (CO), 2200 (CN), 3430 (NH_2). − MS (70 eV); *m/z* (%): 370 [M^+] (13.3), 287 (12.7), 252 (33.9). − $C_{21}H_{11}FN_4O_2$: calcd. C 68.11, H 2.99, N 15.13; found C 68.15, H 3.03, N 15.16.

3-Amino-12-(4-chlorophenyl)-10-cyano-2-oxopyrano[4,3-d]-pyrido[1,2-a]benzimidazole (**10b**): Yield 16%; m.p. > 280°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 4.65 (br. s, 2 H), 7.16 (s, 1 H), 7.45 (t, 1 H), 7.52 (d, 2 H), 7.60 (t, 1 H), 7.90 (d, 1 H), 7.94 (d, 2 H), 8.49 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 1700 cm^{-1} (CO), 2210 (CN), 3440 (NH_2). − MS (70 eV); *m/z* (%): 386 [M^+] (27.1), 358 (11.5), 294 (9.7), 138 (69). − $C_{21}H_{11}ClN_4O_2$: calcd. C 65.21, H 2.87, N 14.49; found C 65.38, H 3.00, N 14.16.

3-Amino-12-(4-bromophenyl)-10-cyano-2-oxopyrano[4,3-d]-pyrido[1,2-a]benzimidazole (**10c**): Yield 18%; m.p. > 280°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 7.18 (s, 1 H), 7.46 (t, 1 H),7.61 (t, 1 H), 7.71 (d, 2 H), 7.86 (d, 2 H), 7.92 (d, 1 H), 8.51 (d, 1 H).

− IR (KBr): $\tilde{\nu}$ = 1695 cm^{-1} (CO), 2200 (CN), 3440 (NH_2). − MS (70 eV); *m/z* (%): 431 [M^+] (24). − $C_{21}H_{11}BrN_4O_2$: calcd. C 58.48, H 2.57, N 12.99; found C 58.21, H 2.71, N 13.19.

3-Amino-10-cyano-12-(4-methoxyphenyl)-2-oxopyrano[4,3-d]-pyrido[1,2-a]benzimidazole (**10d**): Yield 14%; m.p. > 280°C. − ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 3.8 (s, 3 H), 6.88 (s, 1 H), 7.06 (d, 2 H), 7.32 (t, 1 H), 7.46 (t, 1 H), 7.70 (d, 1 H), 7.82 (d, 2 H), 8.52 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 1690 cm^{-1} (CO), 2200 (CN), 3400 (NH_2). − MS (70 eV); *m/z* (%): 382 [M^+] (14.7), 298 (13.3). − $C_{22}H_{14}N_4O_3$: calcd. C 69.10, H 3.69, N 14.65; found C 69.26, H 3.79, N 14.25.

3-Amino-10-cyano-12-(4-methylphenyl)-2-oxopyrano[4,3-d]-pyrido[1,2-a]benzimidazole (**10e**): Yield 12%; m.p. > 280°C. − ^{1}H NMR ([D_6]DMSO): δ = 2.09 (s, 3 H), 7.04 (s, 1 H), 7.28−7.48 (m, 4 H), 7.56−7.66 (m, 3 H), 7.82 (br. s, 2 H), 8.49 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 1690 cm^{-1} (CO), 2200 (CN), 3430 (NH_2). − MS (70 eV); *m/z* (%): 366 [M^+] (80), 388 (18.6), 280 (49.2). − $C_{22}H_{14}N_4O_2$: calcd. C 72.12, H 3.85, N 15.29; found C 72.41, H 3.89, N 15.28.

1-(2-Amino-1,3,4-thiadiazol-5-yl)methyl-4-cyano-3-(4-methoxy-phenyl)pyrido[1,2-a]benzimidazole (**11**): Thiosemicarbazide (0.136 g, 1.5 mmol) was added to a solution of **9d** (0.338 g, 1 mmol) in trifluoroacetic acid (5 ml). The reaction mixture was heated at 70°C with stirring for 10 h. After completion of the reaction, it was cooled, poured into ice/water and the solution neutralized with aq. ammonia. The yellow solid obtained was filtered, washed with acetone and crystallized from DMSO/water (1:1). Yield 48%; m.p. 246°C. − ^{1}H NMR ([D_6]DMSO): δ = 3.86 (s, 3 H), 5.12 (s, 2 H), 7.15−7.24 (m, 5 H), 7.36 (t, 1 H), 7.56 (t, 1 H), 7.86 (d, 2 H), 7.92 (d, 1 H), 8.12 (d, 1 H). − IR (KBr): $\tilde{\nu}$ = 2220 cm^{-1} (CN), 3440 (NH_2). − MS (70 eV); *m/z* (%): 412 [M^+] (4.5), 356 (14.9), 338 (100). − $C_{22}H_{16}N_6OS$: calcd. C 64.06, H 3.91, N 20.38; found C 63.73, H 3.96, N 20.31.

[1] Y. Shiokawa, A. Akahane, H. Katayama, T. Mitsunaga, *Eur. Pat.EP* 299,209, **1989**; *Chem. Abstr.* **1989**, *111*, 134140q.
[2] S. Kakehi, S. Ito, *Jpn. Kokai Tokkyo Koho, JP* 6,197,285, **1986**; *Chem. Abstr.* **1986**, *105*, 208877k.
[3] [3a] E. Badawey, T. Kappe, *Eur. J. Med. Chem*. **1995**, *30*, 327. − [3b] E. S. A. M. Badawey, S. M. Rida, F. S. G. Soliman, T. Kappe, *Monatsh. Chem*. **1987**, *120*, 73.
[4] K. T. Potts, U. P. Singh, J. Bhattacharyya, *J. Org. Chem*. **1968**, *33*, 3766.
[5] R. Krischke, R. Grashey, R. Huisgen, *Liebigs Ann. Chem*. **1977**, 498.
[6] R. Huisgen, R. Grashey, R. Krischke, *Tetrahedron Lett*. **1962**, 387.
[7] T. Sasaki, K. Kanematsu, A. Kakehi, *J. Org. Chem*. **1971**, *36*, 2978.
[8] C. W. Rees, M. Yelland, *J. Chem. Soc., Perkin Trans. 1* **1973**, 221.
[9] A. H. H. Elghandour, M. R. H. Elmoghayar, *J. Prakt. Chem*. **1988**, *330*, 657.
[10] T. Zimmermann, *J. Prakt. Chem*. **1993**, *335*, 717.
[11] [11a] V. J. Ram, M. Verma, F. A. Hussaini, A. Shoeb, *J. Chem. Res.(S)* **1991**, 98. − [11b] V. J. Ram, M. Verma, F. A. Hussaini, A. Shoeb, *Liebigs Ann. Chem*. **1991**, 1229.
[12] V. J. Ram, S. K. Singh, F. A. Hussaini, A. Shoeb, *J. Chem. Res. (S)* **1993**, 110.
[13] F. A. Hussaini, Pragya; M. Nath, S. K. Singh, V. J. Ram, A. Shoeb, A. P. Bhaduri, *J. Chem. Res.* **1994**, 86.
[14] V. J. Ram, S. Mumtazuddin, Pragya, N. Haque, F. A. Hussaini, A. Shoeb, A. P. Bhaduri, *J. Chem. Res. (S)* **1994**, 354.
[15] Y. Tominaga, A. Ushirogochi, Y. Matsuda, G. Kobayashi, *Chem. Pharm. Bull.* **1984**, *32*, 3384.

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