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Synthesis of Functionalized 4*H*-Pyrano[3,2-*c*]pyridines from 4-Hydroxy-6-methyl-2-pyridone and Their Reactions. Unexpected New Routes to 3,3′-Benzylidenebis[4-hydroxy-6-methyl-2(1*H*)-3-pyridinone]s

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The reaction of 4-hydroxy-6-methyl-2-pyridone **1** with benzylidenemalononitriles in an ethanolic solution containing a catalytic amount of piperidine and α-cyanoacrylic esters in pyridine affords the corresponding 4*H*-pyrano[3,2-*c*]pyridines. However, it's reaction with 3-(cyanomethylene)-2-indolinones gives either 2-amino-3-quinolinecarbonitriles or ethyl 2-amino-5′,6′-dihydro-7′-methyl-2,5′-dioxospiro-[indoline-3,4′-[4*H*]-pyrano[3,2-*c*]pyridine-3′-carboxylate. In contrast, the reaction of **1** with 3-aryl-2-cyano-2-propenethioamides affords 3,3′-benzylidenebis[4-hydroxy-6-methyl-2(1*H*)-3-pyridinone]s. The reaction of the obtained 4*H*-pyrano[3,2-*c*]pyridines with acetic anhydride affords the corresponding fused system.

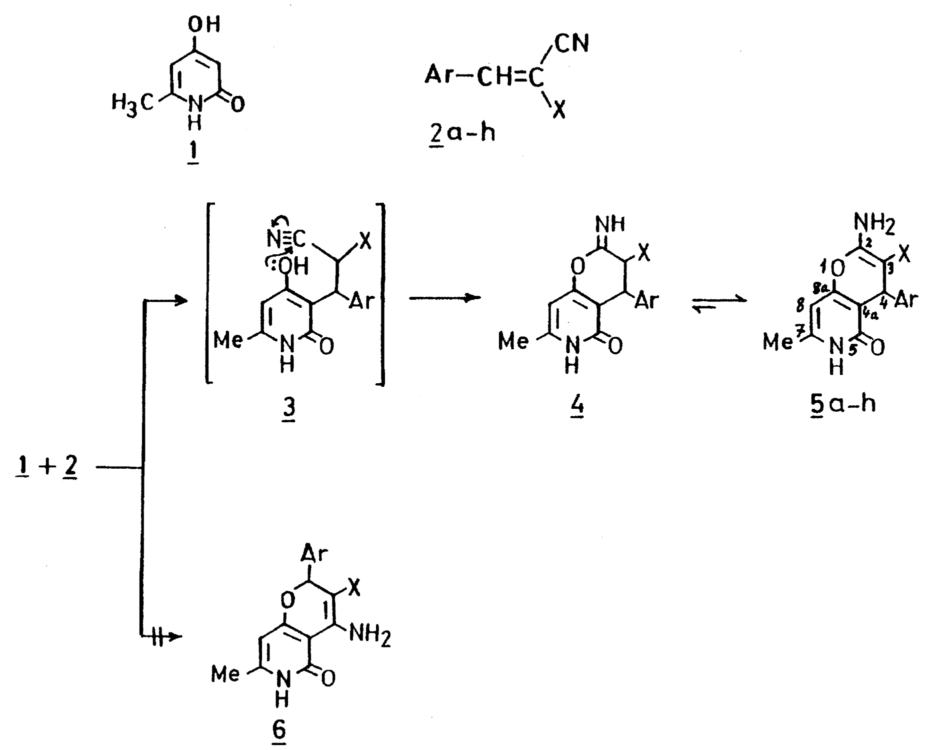
Pyridines are an important class of biologically active compounds, since many pyridine derivatives have proven to posses analgesic and anti-inflammatory properties, and have shown activity against diabetus millilus.[1,2] Owing to the importance of this class of heterocycles and as a part of our program aimed at the development of a new simple, efficient and one-step procedure for the synthesis of pyridine derivatives,[3,4] which are considered to be very important intermediates for the synthesis of various pyrido[2,3-*b*]pyrazine analogous to pteridine and folic acid ring systems,[5,6] we wish to report here on a convenient synthesis of hitherto unknown polyfunctionally substituted pyrano[3,2-*c*]pyridines and some new heterocyclic compounds utilizing the 4-hydroxy-2-pyridones **1** as the starting material. The pyrano[3,2-*c*]pyridine system has almost been neglected, and only a few examples are known.[7,8] Therefore, it seems to be very interesting to synthesize pyrano[3,2-*c*]pyridines in high yields by a convenient method from simple laboratory reagents.

Thus, it has been found that **1** reacts with benzylidenemalononitriles **2a**—**e** in an ethanolic solution containing a catalytic amount of piperidine at reflux temperature to yield 1 : 1 adducts, for which two isomeric structures, **5** and **6**, seemed to be possible. Structure **5** was preferred over the possible isomer **6** based on the ^{1}H NMR spectra, which revealed the amino protons at $\delta = 6.97$—7.20 ppm and the presence of a signal at $\delta = 4.0$—4.5 ppm for one proton linked with an sp^{3} carbon, assignable for 4*H*-pyrans.[9,10] If structure **6** is reaction product, the signal of 2*H*-pyran should have appeared at a lower field as the results of a ring oxygen anisotropic effect. The formation of **5** may take place through the addition of the C-3 position of the pyridine ring to the activated double bond in **2**, followed by the favored "6-exo-dig cyclization"[11] of the intermediate **3** to yield the imino compound **4**, which tautomerizes to the more stable enamino system **5** (Chart 1).

When **1** was subjected to react with α-cyanoacrylic esters **2f**—**h** under various conditions, the expect pyranopyridines did not form, and the starting materials were recovered. We then tried the reaction under more basic conditions and higher reaction temperatures. Thus, the reaction of **1** with **2f**—**h** in refluxing pyridine afforded 1 : 1 reaction products **5f**—**h** based on the spectral data. The IR spectra showed the absence of absorption bands at 2200 and 1760 cm^{-1}, characteristic of the cyano and lactone carbonyl groups,[12] respectively. In addition, the ethyl ester protons, 4*H*-pyran and two amino protons could be detected by ^{1}H NMR.

As an extention of our studies, we have been interested in seeing whether a reaction of this type can be extended to include the behavior of **1** and 3-(cyanomethylene)-2-indolinones **7a**,**b**.

Thus, reacting **1** with an equimolar amount of **7a** in ethanol, catalyzed with a few drops of piperidine, at reflux temperature gave a new spiroheterocylic system **10**, presumbly by a mechanism similar to that discussed above for the formation of **5**. Product **10** was assigned to this structure on the basis of analytical and spectral data. This product showed the absence of a CN band and the appearance of absorption bands at 3450, 3300, 3150, and 1710 cm^{-1} assigned for an amino function and ester carbonyl group. ^{1}H NMR spectrum also exhibited the presence of ethyl ester protons and a NH$_2$ group. Furthermore, its ^{13}C NMR spectra gave strong evidence for the formation of this spiro compound **10**, which revealed one quaternary sp^{3} carbon signal at $\delta = 47.0$ ppm. This signal was assigned to the indoline C-3 (spiro carbon).



2, 5	Ar	X
a	ph	CN
b	4-Cl-C$_6$H$_4$	CN
c	4-OCH$_3$-C$_6$H$_4$	CN
d	4-NO$_2$-C$_6$H$_4$	CN
e	3-NO$_2$-C$_6$H$_4$	CN
f	ph	CO$_2$Et
g	4-Cl-C$_6$H$_4$	CO$_2$Et
h	4-OCH$_3$-C$_6$H$_4$	CO$_2$Et

Chart 1.

Other carbons at $\delta = 95.3$, 145.7, and 159.7 ppm also appeared, which were assigned to pyran C-3, pyran C-6 and the enamine carbon (pyran C-2) of the pyran moiety in **10**, respectively.

In contrast to the behavior of **7a**, compound **7b** was reacted with **1** under the same reaction conditions to yield a product whose structure was assumed to be **12** or **13** (cf. Chart 2). The 2-amino-3-quinolinecarbonitriles **12** were preferred over the possible spiro isomer **13** based on the spectroscopic data. Its IR spectrum showed the presence of an ester carbonyl group at 1720 cm^{-1}. The ^{1}H NMR spectrum of **12** exhibited two singlet signals due to the NH$_2$ protons and pyridine NH at $\delta = 7.18$ and 10.40 ppm, respectively. Additional support for structure **12** was obtained from the ^{13}C NMR spectrum data, which revealed quinoline C-3, the enamine carbon (quinoline C-2), quinoline C-4, and the ester carbonyl carbon at $\delta = 118.9$, 169.1, 172.2, and 187.9 ppm, respectively (cf. Experimental). These spectroscopic results and an elemental analysis allowed us unequivocally to assign structure **12**. We assumed that **12** would be formed though an intramolecular cyclization of the intermediate **11**, which was derived from **7b** through a ring-opening reaction induced by a nucleophilic attack of the 4-hydroxy function in **1** on the 2-indolinone C=O group in **7b** (cf. Chart 2).

For a further investigation of the scope of this reaction, to synthesize pyrano[3,2-*c*]pyridine derivatives, we studied another model system of β-arylacrylonitriles. Thus, the reaction of 3-aryl-2-cyano-2-propenethioamides **14a**—**c** with **1** in ethanol containing a catalytic amount of triethylamine, at reflux temperature, for 5 h did not afford the pyrano[3,2-*c*]pyridines **15**, but furnished instead the unexpected 3, 3′-benzylidenebis[4-hydroxy-6-methyl-2(1*H*)-pyridinone]s **19a**—**c**. Beside the analytical and spectroscopic proofs of the structures of **19a**—**c** (cf. Experimental), they were also proven chemically by an independent synthesis by another route involving refluxing **1** with aromatic aldehydes **17a**—**c**, under the same reaction conditions, to yield **19a**—**c** through the intermediate **18**, as shown in Chart 3. The formation of

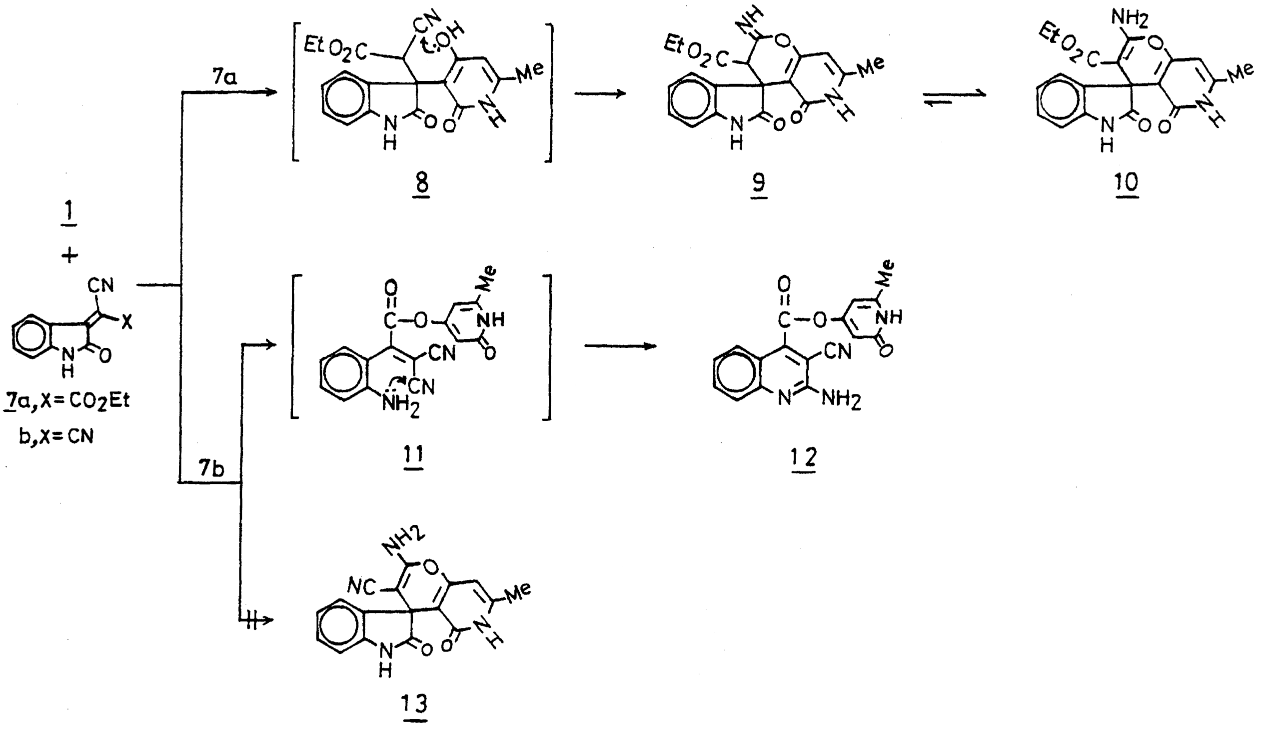


Chart 2.

19 from the reaction of **1** and **14** is assumed to proceed via the addition of pyridine C-3 to the activated double bond in **14** to yield intermediate **16**, which undergoes a retro-Michael elimination to **18**. A subsequent conjugate attack by pyridone **1** leads to **19** (cf. Chart 3). The isolation of **19** indicates that susceptibility to the retro-Michael reaction is a characteristic of the pyridones **1**. Attempts to obtain arylmethanes **19** by the reaction of **1**, aromatic aldehydes and cyanothioacetamide (ternary condensation procedure) under various reaction conditions have not been successful.

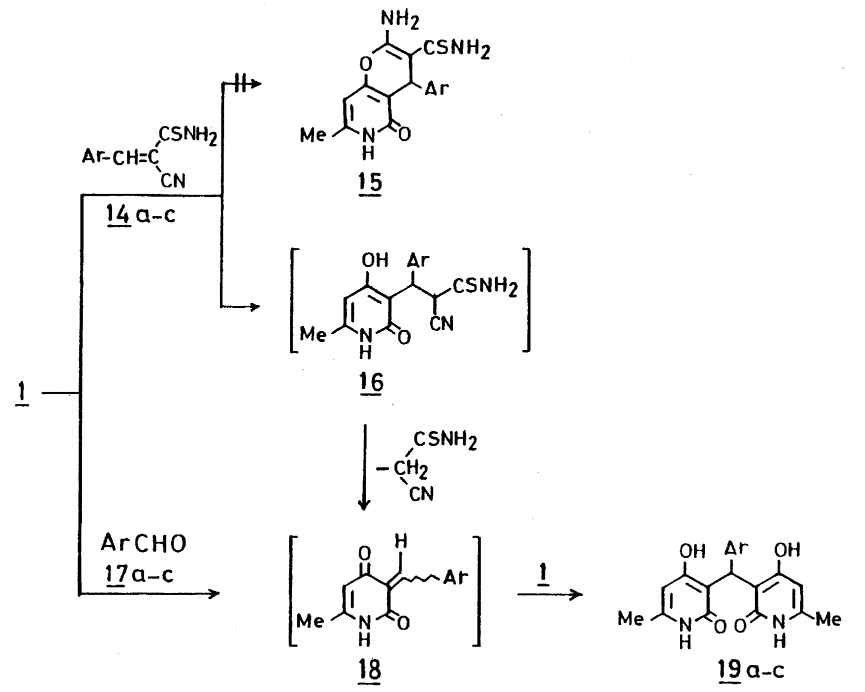
Pyrano[3,2-*c*]pyridines **5a**, **f** were subjected to further reactions to produce fused heterotricyclic systems incorporating a pyrimidine nucleus in addition to the pyranopyridine moiety. Thus, compound **5a** was allowed to react with acetic anhydride at reflux temperature for 11 h, and products **20** and **21** were isolated (Chart 4). Acetylation of compound **5a** may afford a ring-formation product or exocyclic *N*-acetylated products. The exocyclic *N*-acetylated product **20** was assumed to be formed, since the ^{1}H NMR spectrum showed no NH_2 signal at the expected value of $\delta = 6.97$—7.20 ppm and the presence of pyridine NH at $\delta = 11.62$ ppm, in addition to the two methyl groups, 4*H*-pyran, CH at C-5 in the pyridine ring and the exocyclic NH group (see Experimental). However, the reaction of **5f** with Ac_2O, under the same reaction conditions afforded only the exocyclic *N*-acetylated product **22**. Its structure was confirmed on the basis of an elemental analysis and the spectral data (see Experimental).

In an attempt to obtain the desired pyrimidine-fused compound **23**, we first tried the reaction of **5a**, **f** with phenyl isothiocyanate under reflux in benzene; dioxane or toluene/triethylamine, for extended periods. However, the expected reaction did not proceed, and the starting materials were recovered. We then repeated the reaction in a solvent having a higher boiling point, such as *N*,*N*-dimethylformamide (DMF). When **5a**, **f** and phenyl isothiocyanate were refluxed in DMF for 8 h, it also failed to yield **23**, but instead formed an unexpected product, which was shown to be same as the product obtained from the reaction of **1** with **14a**; viz. product **19a**; based on its mps and spectral data. A mechanistic proposal for the formation of this product **19a** involves a nucleophilic attack of H_2O (probably present in solvent) on the pyran ring to form a ring-opened intermediate **24**. Then, the mechanism steps proceed in a way similar to that discussed above concerning the formation of **19** from **1** and **14** (cf. Chart 5). On the other hand, when compounds **5a**, **f** were heated in boiling DMF and in the absence of PhNCS, product **19a** was also obtained.

To our knowledge, this is the first repoted conversion of pyrano[3,2-*c*]pyridines into 3,3′-(arylmethylene)bis[4-hydroxy-6-methyl-2(1*H*)-pyridinone]s. The results indicate that 4-hydroxy-2-pyridones **1** is an excellent starting material for the synthesis of heterocyclic compounds, which are not otherwise readily accessible.

Experimental

All mps were recorded on a Gallen Kamp apparatus, and are uncorrected. IR spectra were obtained (KBr) on a Shimadzu 470 spectrophotometer. ^{1}H NMR spectra were measured on a JEOL Fx-90Q (90 MHz) or JEOL 400 (400 MHz) spectrometer in $(CD_3)_2SO$ using TMS as an internal standard; the chemical shifts are expressed as δ values (ppm). ^{13}C NMR spectra were measured on a Varian XL-300 (300 MHz) spectrometer. Microanalyses were performed by the Microanalytical Data Unit at Cairo University. Mass spectra were determined on a Hitachi M-80 double focusing mass spectrometer at 70 eV. For analytical TLC, silica gel 60 F254 (Merck)



14, 17, 19	Ar
a	ph
b	4-Cl-C_6H_4
c	4-OCH_3- C_6H_4

Chart 3.

was used.

Synthesis of Pyrano[3,2-*c*]pyridines 5a—h; Spiro[indoline-3,4′-[4*H*]pyrano[3,2-*c*]pyridine] Derivatives 10 and 2-Amino-quinoline-3-carbonitrile Derivative 12. A mixture of **1** (2.4 mmol) and **2a**—**e** or **7a**, **b** (2.4 mmol) was refluxed in absolute ethanol (15 ml), containing a catalytic amount of piperidine for 2—4 h (TLC control). After concentration and cooling at room temperature, the resulting solid product was collected by filtration, washed with a small amount of ethanol and dried. Compounds **5f**—**h** were prepared following the same procedure in refluxing pyridine.

2-Amino-5,6-dihydro-7-methyl-5-oxo-4-phenyl-4*H*-pyrano-[3,2-*c*]pyridine-3-carbonitrile (5a). Colorless crystals from DMF, Yield 93%, mp 293—295 °C (decomp). IR ν 3450, 3350, 3150 (NH), 2200 (CN), 1660 (CO), and 1630 (C=N) cm^{-1}; ^{1}H NMR $\delta=2.16$ (s, 3H, CH_3), 4.3 (s, 1H, pyran CH-4), 5.87 (s, 1H, pyridine CH-5), 6.98 (s, 2H, NH_2), 7.10—7.35 (m, 5 Ar-H), 11.51 (s, 1H, NH), ^{13}C NMR $\delta=18.2$ (CH_3), 57.8 (C-4), 95.8 (C-3), 106.3 (C-8), 120 (CN), 126.5—128.3 (aromatic carbons), 144.9 (C-4a), 145.7 (C-7), 156.6 (C-8a), 159.2 (C-2), 161.7 (CO). MS *m*/*z* (%) 279 (100) [M$^+$]. Found: C, 68.72; H, 4.70; N, 14.91%. Calcd for $C_{16}H_{13}N_3O_2$ (279.28): C, 68.80; H, 4.69; N, 15.05%.

2-Amino-5,6-dihydro-7-methy-5-oxo-4-(4-chlorophenyl)-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (5b). Yellow crystals from EtOH, Yield 84%, mp 264—266 °C (decomp). IR ν 3450, 3300, 3200 (NH), 2200 (CN), 1660 (CO), and 1620 (C=N) cm^{-1}; ^{1}H NMR $\delta=2.15$ (s, 3H, CH_3), 4.3 (s, 1H, pyran CH-4), 5.88 (s, 1H, pyridine CH-5), 7.0 (s, 2 H, NH_2), 7.15 (d, $J=3$ Hz, 2 Ar-H), 7.35 (d, $J=3$ Hz, 2 Ar-H), 11.55 (s, 1H, NH); ^{13}C NMR $\delta=18.2$ (CH_3), 57.3 (C-4), 95.9 (C-3), 105.7 (C-8), 119 (CN), 128.2—131.1 (aromtic carbons), 143.9 (C-4a), 145.9 (C-7), 156.6 (C-8a), 159.2 (C-2), 161.7 (CO). MS *m*/*z* (%) 313/315 (100) [M$^+$]. Found: C, 61.19; H, 4.02; Cl, 11.29; N, 13.55%. Calcd for $C_{16}H_{12}ClN_3O_3$ (313.78): C, 61.24; H, 3.85; Cl, 11.31; N, 13.39%.

2-Amino-5,6-dihydro-7-methyl-5-oxo-4-(4-methoxyphenyl)-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (5c). Colorless crystals from DMF/EtOH, Yield 84%, mp 250—251 °C. IR ν 3450, 3300, 3150 (NH), 2200 (CN), 1660 (CO), and 1630 (C=N) cm^{-1}; ^{1}H NMR $\delta=2.2$ (s, 3H, CH_3), 3.7 (s, 3H, OCH_3), 4.25 (s, 1H, pyran CH-4), 5.88 (s, 1H, pyridine CH-5), 6.84 (d, $J=3$ Hz, 2 Ar-H), 6.97 (s, 2H, NH_2), 7.07 (d, $J=3$ Hz, 2 Ar-H), 11.5 (s, 1H, NH). Found: C, 65.89; H, 5.08; N, 13.74% Calcd for $C_{17}H_{15}N_3O_3$ (309.31): C, 66.01; H, 4.89; N, 13.58%.

2-Amino-5,6-dihydro-7-methyl-5-oxo-4-(4-nitrophenyl)-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (5d). Yellow crystals from DMF/EtOH, Yield 62%, mp 290—291 °C (decomp). IR ν 3350, 3300, 3150, (NH), 2200 (CN) 1660 (CO), and 1620 (C=N) cm^{-1};^{1}H NMR $\delta=2.2$ (s, 3H, CH_3), 4.5 (s, 1H, pyran CH-4), 5.93 (s, 1H, pyridine CH-5), 7.15 (s, 2H, NH_2), 7.45 (d, $J=4.5$ Hz, 2 Ar-H), 8.17 (d, $J=4.5$ Hz, 2 Ar-H), 11.6 (s, 1H, NH). Found: C, 59.23; H, 3.82; N, 17.11%. Calcd for $C_{16}H_{12}N_4O_4$ (324.28): C, 59.26; H, 3.73; N, 17.27%.

2-Amino-5,6-dihydro-7-methyl-5-oxo-4-(3-nitrophenyl)-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (5e). Colorless crystals

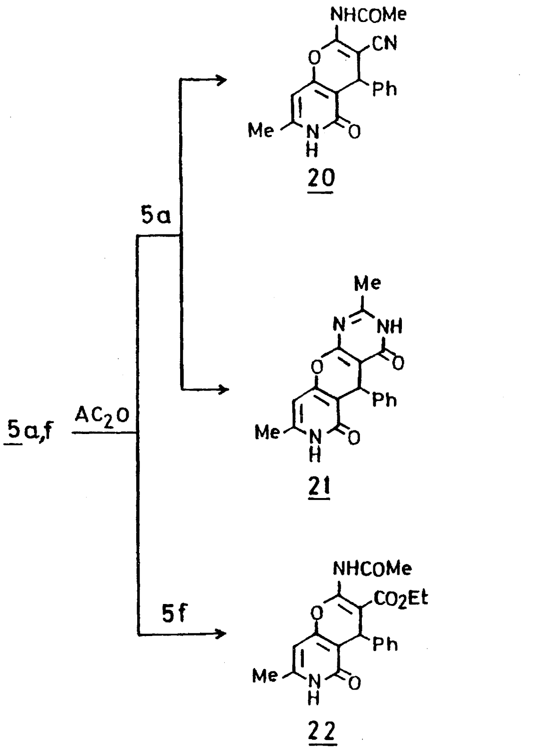


Chart 4.

from DMF, Yield 92%, mp 309—310 °C. IR ν 3450, 3350, 3150 (NH), 2200 (CN), 1660 (CO), and 1620 (C=N) cm^{-1}; ^{1}H NMR $\delta = 2.2$ (s, 3H, CH$_3$), 4.58 (s, 1H, pyran CH-4), 5.93 (s, 1H, pyridine CH-5), 7.2 (s, 2H, NH$_2$), 7.55—7.75 (m, 2 Ar-H), 7.94—8.13 (m, 2 Ar-H), 11.6 (s, 1H, NH). MS *m/z* (%) 324 (8) [M$^+$]. Found: C, 59.18; H, 3.90; N, 17.19%. Calcd for $C_{16}H_{12}N_4O_4$ (324.28): C, 59.26; H, 3.73; N, 17.27%.

Ethyl 2-Amino-5,6-dihydro-7-methyl-5-oxo-4-phenyl-4*H*-pyrano[3,2-*c*]pyridine-3-carboxylate (5f). Colorless crystals from EtOH, Yield 56%, mp 225—227 °C. IR ν 3350, 3300, 3200, (NH), 1680 (CO), 1640 (CO), and 1580 (C=N) cm^{-1}; ^{1}H NMR $\delta = 1.1$ (t, $J = 3$ Hz, 3H, CH$_3$), 2.15 (s, 3H, CH$_3$), 4.0 (q, $J = 3$ Hz, 2H, CH$_2$), 4.65 (s, 1H, pyran CH-4), 5.9 (s, 1H, pyridine CH-5), 7.1—7.3 (m, 5 Ar-H), 7.6 (s, 2H, NH$_2$), 11.47 (s, 1H, NH); ^{13}C NMR $\delta = 15.7$ (ester CH$_3$), 19.8 (CH$_3$), 57.4 (C-4), 60.1 (ester CH$_2$), 97.2 (C-3), 110.7 (C-8), 127—129.1 (aromatic carbons), 146.3 (C-4a), 147.9 (C-7), 157.8 (C-8a), 161.3 (C-2), 163.3 (CO), 169.5 (ester CO). MS *m/z* (%) 326 (14) [M$^+$]. Found: C, 66.35; H, 5.47; N, 8.66%. Calcd for $C_{18}H_{18}N_2O_4$ (326.34): C, 66.24; H, 5.56 ; N, 8.58 %.

Ethyl 2-Amino-5,6-dihydro-7-methyl-5-oxo-4-(4-chlorophenyl)-4*H*-pyrano[3,2-*c*]pyridine-3-carboxylate (5g). Yellow crystals from EtOH, Yield 48%, mp 224—226 °C. IR ν 3400, 3300 3150 (NH), 1680 (CO), 1640 (CO), and 1580 (C=N) cm^{-1}; ^{1}H NMR $\delta = 1.1$ (t, $J = 3$ Hz, 3H, CH$_3$), 2.2 (s, 3H, CH$_3$), 4.0 (q, $J = 3$ Hz, 2H, CH$_2$), 4.65 (s, 1H, pyran CH-4), 5.9 (s, 1H, pyridine CH-5), 7.13—7.32 (m, 4 Ar-H), 7.65 (s, 2H, NH$_2$), 11.5 (s, 1H, NH). Found: C, 60.08; H, 4.82; Cl, 9.72; N, 7.61%. Calcd for $C_{18}H_{17}ClN_2O_4$ (360.83): C, 59.91; H, 4.75; Cl, 9.84; N, 7.76%.

Ethyl 2-Amino-5,6-dihydro-4-(4-methoxyphenyl)-7-methyl-5-oxo-4*H*-pyrano[3,2-*c*]pyridine-3-carboxylate (5h). Colorless crystals from DMF/EtOH, Yield 52%, mp 234—236 °C. IR ν 3400, 3300, 3150 (NH), 1690 (CO), 1650 (CO), and 1590 (C=N) cm^{-1}; ^{1}H NMR $\delta = 1.1$ (t, $J = 3$ Hz, 3H, CH$_3$), 2.1 (s, 3H, CH$_3$), 3.65 (s, 3H, OCH$_3$), 3.95 (q, $J = 3$ Hz, 2H, CH$_2$), 4.7 (s, 1H, pyran CH-4), 5.7 (s, 1H, pyridine CH-5), 6.63 (d, $J = 3$ Hz, 2 Ar-H), 7.1 (s, 2H, NH$_2$), 7.2 (d, $J = 3$ Hz, 2 Ar-H), 11.35 (s, 1H, NH). Found: C, 63.96; H, 5.72; N, 7.89%. Calcd for $C_{19}H_{20}N_2O_5$ (356.36): C, 64.03; H, 5.66; N, 7.86%.

Ethyl 2-Amino-5′,6′-dihydro-7′-methyl-2,5′-dioxospiro[indoline-3,4′-[4*H*]-pyrano[3,2-*c*]pyridine]-3′-carboxylate (10). Red crystals from DMF, Yield 86%, mp 310—312 °C. IR ν 3450, 3300, 3150 (NH), 1710 (CO), 1680 (CO), 1640 (CO), and 1610 (C=N) cm^{-1}; ^{1}H NMR $\delta = 0.82$ (t, $J = 3$ Hz, 3H, CH$_3$), 2.12 (s, 3H, CH$_3$), 3.7 (q, $J = 3$ Hz, 2H, CH$_2$), 5.85 (s, 1H, pyridine CH-5), 6.7—6.95 (m, 3 Ar-H), 7.08 (m, 1 Ar-H), 7.9 (s, 2H, NH$_2$), 10.2 (s, 1H, indole NH), 11.3 (s, 1H, pyridine NH); ^{13}C NMR $\delta = 13.2$ (ester CH$_3$), 18.2 (CH$_3$), 47.0 (spiro carbon), 58.8 (ester CH$_2$) 95.3 (pyran C-3), 106.3 (pyran C-5), 107.9 (pyridine C-3), 120—127 (aromatic carbons), 135.9 (indole C-3a), 144.5 (indole C-7a), 145.7 (pyran C-6), 156.3 (pyridine C-6), 159.7 (pyran C-2), 160.6 (pyridine C-2), 167.9 (ester CO), 179.8 (indole C-2). MS *m/z* (%) = 367 (29) [M$^+$]. Found: C, 61.98; H, 4.81; N, 11.66%. Calcd for $C_{19}H_{17}N_3O_5$ (367.35): C, 62.12; H, 4.67; N, 11.44%.

2-Amino-4-{[(1,2-dihydro-6-methyl-2-oxo-4-pyridyl)oxy]car-

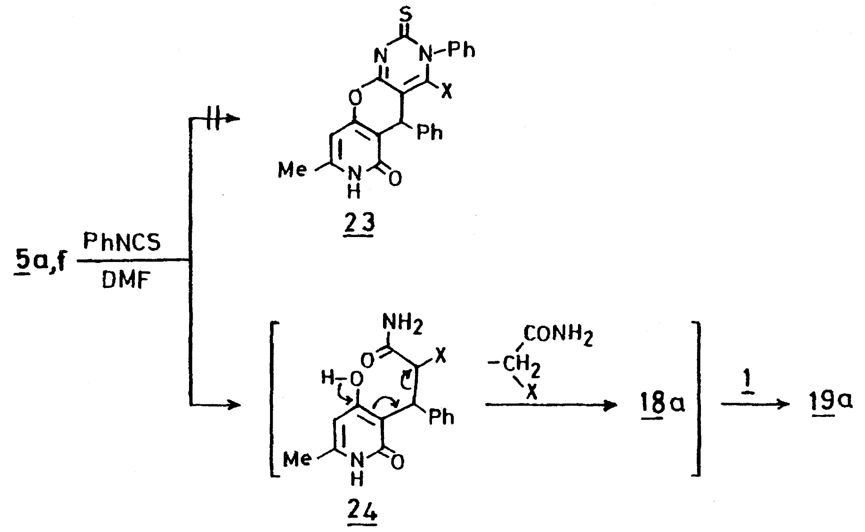


Chart 5.

bonyl}-3-quinolinecarbonitrile (12). Colorless crystals from DMF, Yield 95%, mp > 360 °C. IR ν 3500, 3200 (NH), 2200 (CN), 1720 (ester CO), 1660 (CO), and 1600 (C=N) cm^{-1}; ^{1}H NMR $\delta = 2.15$ (s, 3H, CH_3), 5.9 (s, 1H, pyridine CH-5), 6.75—6.97 (m, 3H, 2 Ar-H and pyridine CH-5), 7.09—7.22 (m, aromatic and NH_2), 8.0 (s, 1 Ar-H), 11.4 (s, 1H, NH); ^{13}C NMR $\delta = 28.2$ (CH_3), 67.0 (pyridine C-3), 105.5 (pyridine C-5), 113.6 (CN), 118.9 (quinoline C-3), 127.6—137.9 (aromatic carbons), 144.4 (quinoline C-4a), 152.3 (pyridine C-6), 156.3 (quinoline C-8a), 167.3 (pyridine C-2), 169.1 (quinoline C-2), 170.5 (pyridine C-4), 172.2 (quinoline C-4), 187.9 (ester CO). MS *m*/*z* (%) = 320 (85) [M$^+$]. Found: C, 63.90; H, 3.80; N, 17.43%. Calcd for $C_{17}H_{12}N_4O_3$ (320.29): C, 63.74; H, 3.78; N, 17.49%.

Synthesis of 3,3′-(Arylmethylene)bis[4-hydroxy-6-methyl-2(1*H*)-3-pyridinone]s 19a—c; Method A. To solution of **1** (1.6 mmol) in ethanol (10 ml) containing a catalytic amount of triethylamine (1 ml), compound **14a—c** or **17a—c** (1.6 mmol) was then added and the mixture was refluxed for 3—5 h (TLC control). After concentration and cooling to room temperature, the resulting solid product was collected by filtration, washed with methanol and dried.

Method B for 19a: A solution of **5a**, **f** (1 mmol) in DMF (5 ml) was refluxed for 8—10 h (TLC control). After concentration and cooling, the resulting solid was collected by filtration, washed with methanol and dried.

3,3′-Benzylidenebis[4-hydroxy-6-methyl-2(1*H*)-3-pyridinone] (19a). Yield 14% (method A) and 35% (method B), mp 335—337 °C (decomp) (Lit,[13] 325—327 °C).

3,3′-(4-Chlorophenylmethylene)bis[4-hydroxy-6-methyl-2(1*H*)-3-pyridinone] (19b). Colorless crystals from DMF, Yield 44%, mp 320—322 °C. IR ν 3300—2600 (NH) and 1660 (CO) cm^{-1}; ^{1}H NMR $\delta = 2.16$ (s, 6H, $2CH_3$), 5.90 (s, 1H, CH), 5.95 (s, 2H, 2 pyridine CH-5), 7.02 (d, $J = 3$ Hz, 2 Ar-H), 7.3 (d, $J = 3$ Hz, 2, ArH), 11.7 (s, 2H, 2NH). Found: C, 61.43; H, 4.44; Cl, 9.56; N, 7.40%. Calcd for $C_{19}H_{17}ClN_2O_4$ (372.84): C, 61.20; H, 4.60; Cl, 9.52; N, 7.51%.

3,3′-(4-Methoxyphenylmethylene)bis[4-hydroxy-6-methyl-2(1*H*)-pyridinone] (19c). Colorless crystals from DMF; Yield 46%, mp 301—303 °C. IR ν 3300—2600 (NH) and 1660 (CO) cm^{-1}; ^{1}H NMR $\delta = 2.16$ (s, 6H, $2CH_3$), 3.70 (s, 3H, OCH_3), 5.85 (s, 1H, CH), 5.97 (s, 2H, 2 pyridine CH-5), 6.78 (d, $J = 3$ Hz, 2 ArH), 6.90 (d, $J = 3$ Hz, 2ArH), 11.66 (s, 2H, 2NH); ^{13}C NMR $\delta = 19.6$ (CH_3), 34.5 (CH), 56.3 (OCH_3), 103.3 (C-5), 114.7 (C-3), 128.7—131.9 (aromatic carbons), 145.6 (C-6), 158.5 (C-4), 163.5 (C-2). MS *m*/*z* (%) 368 (100) [M$^+$]. Found: C, 65.19; H, 5.41; N, 7.72%. Calcd for $C_{20}H_{20}N_2O_5$ (368.37): C, 65.21; H, 5.47; N, 7.60%.

Reaction of 5a,f with Acetic Anhydride. A solution of **5a** (1.8 mmol) in acetic anhydride (10 ml) was refluxed for 11 h (TLC control). The excess acetic anhydride was removed in vacuo, and the residue was chromatographed as a preparative TLC using (Acet. : $CH_2Cl_2 = 3:7$) as an eluent to give two zones. Extraction with acetone gave compounds **20** and **21**. Under similar conditions, compounds **5f** (0.92 mmol) was refluxed for 11 h, then cooled and poured into an ice/H_2O mixture. The resulting solid *N*-acetylated product **22** was filtered off, washed several times with H_2O and dried.

2-Acetamido-5,6-dihydro-7-methyl-5-oxo-4-phenyl-4*H*-pyrano[3,2-*c*]pyridine-3-carbonitrile (20). Buff crystals from MeOH; Yield 23%, mp 147—149 °C. IR ν 3300—3150 (NH), 2200 (CN), 1670 (CO), and 1630 (CO) cm^{-1}; ^{1}H NMR $\delta = 2.05$ (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 4.57 (s, 1H, pyran CH-4), 5.94 (s, 1H, pyridine CH-5), 7.24—7.32 (m, 5Ar-H), 10.59 (s, 1H, acetamido NH), 11.62 (s, 1H, pyridine NH). Found: C, 67.30; H, 4.92; N, 12.98%. Calcd for $C_{18}H_{15}N_3O_3$ (321.32): C, 67.28; H, 4.70; N, 13.08%.

2,8-Dimethyl-5-phenyl-5,7-dihydro-4*H*-pyrido[3,4:5,6]pyrano[2,3-*d*]pyrimidine-4,6-(3*H*)-dione (21). Colorless crystals from DMF; Yield 35%, mp > 360 °C. IR ν 3300—2600 (NH), 1660 (CO), and 1640 (CO) cm^{-1}; ^{1}H NMR $\delta = 2.15$ (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 4.82 (s, 1H, pyran CH-4), 6.02 (s, 1H, pyridine CH-5), 7.11—7.21 (m, 5 Ar-H), 11.49 (s, 1H, pyridine NH), 12.49 (s, 1H, pyrimidine NH). Found: C, 67.15; H, 4.67; N, 13.28%. Calcd for $C_{18}H_{15}N_3O_3$ (321.32): C, 67.28; H, 4.70; N, 13.08%.

Ethyl 2-Acetamido-5,6-dihydro-7-methyl-5-oxo-4-phenyl-4*H*-pyrano[3,2-*c*]pyridine-3-carboxylate (22). Brownish crystals from EtOH, Yield 50%, mp 152—154 °C. IR ν 3300—2700 (NH) 1730 (ester CO), and 1680 (CO), 1660 (CO) cm^{-1}; ^{1}H NMR $\delta = 1.12$ (t, $J = 3$ Hz, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 4.0 (q, $J = 3$ Hz, 2H, CH_2), 4.80 (s, 1H, pyran CH-4), 5.93 (s, 1H, pyridine CH-5), 7.14—7.28 (m, 5 Ar-H), 10.26 (s, 1H, acetamido NH), 11.53 (s, 1H, pyridine NH). Found: C, 65.17; H, 5.53; N, 7.41%. Calcd for $C_{20}H_{20}N_2O_5$ (368.37): C, 65.21; H, 5.47; N, 7.60%.

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