

Synthetic approaches towards 5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-ones

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The construction of 5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-ones **2** was achieved through the reaction of 1-aryl-3-(2-hydroxyphenyl)-2-propen-1-ones **1** with malononitrile in alcoholic KOH solution affording the compound **2** along with 2-alkoxy-4-amino-6-aryl-3,5-pyridinedicarbonitriles **3**. Single crystal X-ray diffraction of **3e** confirmed the established structure and excluded the formation of the isomeric product **4**.

Keywords: 2-propen-1-ones, malononitrile, 5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-ones, 3,5-pyridinedicarbonitriles, Michael reaction, Knoevenagel condensation.

The reaction of α,β -unsaturated Michael acceptors with active methylene compounds is a general route for carbon carbon bond formation. Malononitrile is with α,β -unsaturated ketones and either organic¹⁻³ or inorganic^{4,5} basic catalysts to afford open chain adducts. However, reaction of malononitrile with 1,2,3-triaryl-2-propen-1-ones gave the 2-amino-3-cyano-4,5,6-triaryl-4*H*-pyrans. It was assumed that the introduction of an aryl group at the α -position of the Michael acceptor is essential for this cyclization process.^{6,7} Various 2-propen-1-ones also react with malononitrile under basic catalysis to yield cyclohexanol derivatives *via* double Michael reaction of malononitrile with the propenone followed by an intramolecular cyclisation under the basic conditions.^{4,7-9} On the other hand, reaction of 1,3-diaryl-2-propen-1-ones with malononitrile in the presence of a sufficient amount of alkoxide anion led to the formation of 2-alkoxy-3-cyanopyridines.^{7,8,10} Numerous condensed pyridinecarbonitrile systems were obtained using similar conditions by the reaction of malononitrile with various α,β -unsaturated ketones.¹¹⁻¹⁵

In the present work, the reaction of 1-aryl-3-(2-hydroxyphenyl)-2-propen-1-ones with malononitrile in the presence of sufficient amount of alkoxide anion was investigated. The hydroxyl group might behave as an active nucleophilic centre in the reaction affording the condensed 5*H*-[1]benzopyrano[3,4-*c*]pyridine derivatives. The synthesis of this condensed heterocyclic system is interesting due to the potential biological activities associated with its structure such as antipsychotic “dopamine D₄ receptor antagonist”,¹⁶⁻¹⁸ anticholinergic and bronchodilating agents.¹⁹⁻²⁴

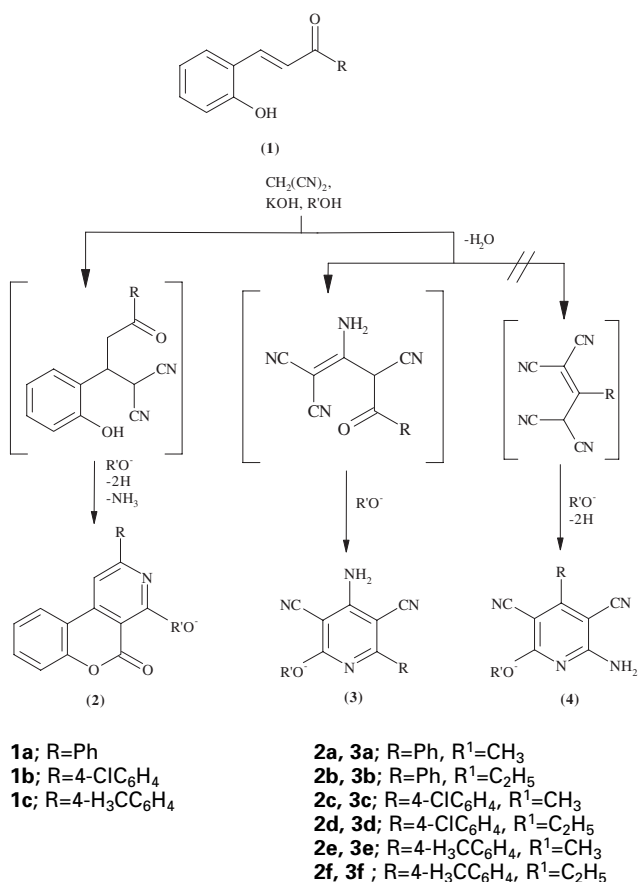
Reaction of 1-aryl-3-(2-hydroxyphenyl)-2-propen-1-ones **1a-c** with malononitrile in alcoholic (methanolic or ethanolic) KOH solution at room temperature, afforded a mixture of two products which were isolated by silica gel TLC. Their structures were established as 4-alkoxy-2-aryl-5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-ones **2** and 2-alkoxy-4-amino-6-aryl-3,5-pyridinedicarbonitriles **3** based on spectroscopic (IR, ¹H, ¹³C NMR, MS) and elemental analyses data.

The IR spectra of **2a-f** did not obtain any absorption assignable to a nitrile vibration. However, a strong band due to carbonyl stretching vibration was observed at $\nu = 1747-1734$ cm⁻¹. The ¹H NMR spectra of **2a-f** showed the presence of an alkoxide residue confirming the involvement of either methoxide (singlet at $\delta = 4.26-4.29$) or ethoxide (triplet at $\delta = 1.51-1.57$, quartet at $\delta = 4.69-4.77$) functions derived from the corresponding alcohol used in the reaction. In addition the heterocyclic H-1 appeared as a sharp singlet signal at $\delta = 7.84-7.98$. ¹³C NMR spectrum of **2b** adds a conclusive support for the established structure revealing the methyl and methylene carbons of ethoxide residue at $\delta = 14.60, 63.30$ respectively,

together with to the heterocyclic C-1 and carbonyl carbons at $\delta = 104.16, 164.18$ respectively.

The formation of **2** was assumed to take place *via* a Michael addition of the active methylene malononitrile to the β -carbon of 2-propen-1-ones **1**. Then, cyclisation due to addition of the alkoxide residue at one of the nitrile groups with subsequent nucleophilic attack of the hydroxyl oxygen at the other nitrile function took place. Hydrolysis of the imino group under these reaction conditions afforded eventually the 4-alkoxy-2-aryl-5*H*-[1]benzopyrano[3,4-*c*]pyridin-5-ones **2** (Scheme 1).

The IR spectra of **3a-f** did not contain any absorption corresponding to a carbonyl function. On the other hand, bands assignable for the amino stretching vibration absorption appeared at $\nu = 3452-3235$ cm⁻¹ beside the nitrile stretching vibration bands at $\nu = 2231-2210$ cm⁻¹. ¹H NMR spectra of **3a-f** exhibited the alkoxide residue (singlet at $\delta = 4.11$ for the methoxide and triplet at $\delta = 1.38-1.44$, quartet at $\delta = 4.50-4.58$ for the ethoxide protons) in addition to the amino singlet



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Scheme 1

signal at $\delta = 5.58\text{--}5.68$. ^{13}C NMR spectrum of **3e** exhibited data consistent with the established structure in which the methoxide carbon appeared at $\delta = 59.87$ in addition to the nitrile carbons at $\delta = 118.47, 120.76$. The pyridine C-5 and C-3 appeared at $\delta = 81.24, 91.79$ respectively.

The formation of **3** presumably, took place through oxidative cleavage of the starting propenone **1** giving rise to the (un) substituted benzoate ester, which in turn interacted with the active methylene malononitrile dimer (formed under the basic reaction conditions). Subsequently, cyclisation took place due to alkoxide nucleophilic attack at one of the nitrile groups finally giving the 2-alkoxy-4-amino-6-aryl-3, 5-pyridine-dicarbonitriles **3**.

Single crystal X-ray diffraction of **3e**²⁵ (Fig. 1) confirms the established structure and excludes the presence of any isomeric product such as **4**.

Single crystal X-ray experimental data of **3e**.

The experimental data were collected at $T = 298$ °K on a Kappa CCD Enraf Nonius FR 590 diffractometer using a graphite monochromator with $M\alpha\text{-K}\alpha$ radiation ($\lambda = 0.71073$ Å). The crystal structure was determined by SIR92²⁶ and refined by maXus²⁷ (Bruker Nonius, Delft and MacScience, Japan). Chemical formula $\text{C}_{15}\text{H}_{12}\text{N}_4\text{O}$, $M_r = 264.288$, monoclinic, crystallizes in space group $P-21/c$, Cell lengths " $a = 6.9467(5)$, $b = 17.7902(12)$, $c = 11.0487(10)$ Å", $\beta = 99.387(2)^\circ$, $V = 1347.1(2)$ Å³, $Z = 4$, $D_c = 1.303$ g/cm³, θ values $2.96\text{--}27.09^\circ$, absorption coefficient μ (Mo-K α) = 0.09 mm⁻¹, $F(000) = 552$. 3670 unique reflections were measured, of which 849 reflections with threshold expression $I > 3\sigma(I)$ were used in the structural analysis. Convergence for 196 variable parameters by least-squares refinement on F^2 with $w = 1/[\sigma^2(F_o^2) + 0.10000 F_o^2]$. The final agreement factors were $R = 0.052$ and $wR = 0.095$ with a goodness-of-fit of 2.107.

Selected intramolecular bond lengths (Å) and bond angles (°) of **3e**: O(1)–C(8)=1.353(3), O(1)–C(18)=1.459(4), N(2)–C(12)=1.343(4), N(3)–C(15)=1.148(4), N(4)–C(7)=1.357(3), N(4)–C(8)=1.326(4), C(5)–C(8)=1.381(4), C(5)–C(12)=1.400(4), C(5)–C(15)=1.435(4), C(6)–C(11)=1.400(5), C(6)–N(13)=1.165(4), C(7)–C(11)=1.406(4), C(7)–C(14)=1.486(4), C(11)–C(12)=1.415(4), N(2)–H(2A)=1.078(3), N(2)–H(2B)=0.82(3), C(18)–H(18A)=1.06(3), C(18)–H(18B)=0.93(3), C(18)–H(18C)=1.010(4), C(8)–O(1)–C(18)=118.7(3), C(7)–N(4)–C(8)=118.0(3), C(8)–C(5)–C(12)=117.6(3), C(8)–C(5)–C(15)=121.4(3), C(12)–C(5)–C(15)=121.1(3), C(11)–C(6)–N(13)=172.9(4), N(4)–C(7)–C(11)=120.4(3), N(4)–C(7)–C(14)=112.9(3), C(11)–C(7)–C(14)=126.7(3), O(1)–C(8)–N(4)=118.4(3), O(1)–C(8)–C(5)=115.7(3), N(4)–C(8)–C(5)=125.9(3), C(6)–C(11)–C(7)=123.2(3), C(6)–C(11)–C(12)=116.2(3), C(7)–C(11)–C(12)=120.5(3), N(2)–C(12)–C(5)=121.4(3), N(2)–C(12)–C(11)=121.2(3), C(5)–C(12)–C(11)=117.5(3), N(3)–C(15)–C(5)=178.0(4), C(12)–N(2)–H(2A)=119.3(3), C(12)–N(2)–H(2B)=123.(2), H(2A)–N(2)–H(2B)=118.(2), O(1)–C(18)–H(18A)=105.(2), O(1)–C(18)–H(18B)=106.(2), O(1)–C(18)–H(18C)=109.5(3).

Experimental

Melting points are uncorrected and recorded on an Electrothermal 9100 melting point apparatus. IR spectra (KBr) were recorded on a Bruker Vector 22 spectrophotometer. NMR spectra were recorded on a Varian MERCURY 300 (^1H : 300 MHz; ^{13}C : 75 MHz) spectrometer. Mass spectra were recorded on a Finnigan SSQ 7000 (EI, 70 eV) spectrometer. The starting compounds **1a–c**²⁸ were prepared according to the previously reported procedures.

Reaction of **1** with malononitrile (general procedure).

A mixture of equimolar amounts of the appropriate **1a–c** and malononitrile (10 mmol) in the corresponding alcohol (25 ml)

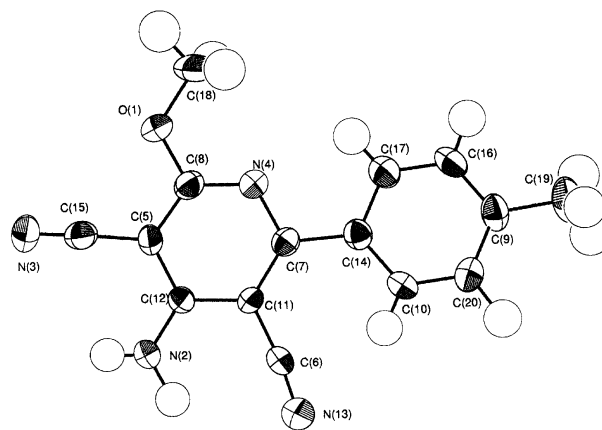


Fig. 1 Single crystal X-ray diffraction of **3e**

containing KOH (1 g) was stirred at room temperature (25–30 °C) for the appropriate time. The solid which separated was collected, washed with water and purified on silica gel TLC (F 254) affording the corresponding **2a–f** and **3a–f** respectively.

4-Methoxy-2-phenyl-5H-[1]benzopyrano[3,4-c]pyridin-5-one (2a): Using the general procedure **1a** (2.24 g; 10 mmol) and malononitrile (0.66 g; 10 mmol) in methanol (25 ml) gave **2a**. With the reaction time of 72h, colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 213–215 °C, yield 20%. IR: ν 1743 (C=O), 1592, 1548 cm⁻¹ (C=N, C=C). ^1H NMR (CDCl_3): δ 4.29 (s, 3H, OCH₃), 7.35–7.58 (m, 6H, arom. H), 7.98 (s, 1H, hetero. H-1), 8.10–8.20 (m, 3H, arom. H). MS: m/z (%) 303 [(M), 100], 288 (2), 274 (46), 273 (12), 272 (5). Anal. for $\text{C}_{19}\text{H}_{13}\text{NO}_3$ (303.297): calcd. C 75.24, H 4.32, N 4.62; found C 75.19, H 4.30, N 4.61%.

4-Ethoxy-2-phenyl-5H-[1]benzopyrano[3,4-c]pyridin-5-one (2b): Using the general procedure **1a** (2.24 g; 10 mmol) and malononitrile (0.66 g; 10 mmol) in ethanol (25 ml) gave **2b**. With a reaction time of 24h. Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 171–173 °C, yield 22%. IR: ν_{max} 1740 (C=O), 1597, 1546 cm⁻¹ (C=N, C=C). ^1H NMR (CDCl_3): δ 1.57 (t, $J = 7.2$ Hz, 3H, CH₃), 4.77 (q, $J = 7.2$ Hz, 2H, OCH₂), 7.31–7.58 (m, 6H, arom. H), 7.92 (s, 1H, hetero. H-1), 8.07–8.17 (m, 3H, arom. H). ^{13}C NMR (CDCl_3) "APT": δ 14.60 (CH₃), 63.30 (OCH₂), 104.16 (hetero. C-1), 117.48, 123.53, 124.06, 127.17, 128.69, 130.30, 132.25 (arom. CH), 102.15, 116.30, 137.51, 145.47, 152.86, 156.82, 159.04 (arom. quaternary C), 164.18 (C=O). MS: m/z (%) 317 [(M), 88], 302 (76), 289 (56), 288 (20), 273 (100), 272 (16). Anal. for $\text{C}_{20}\text{H}_{15}\text{NO}_3$ (317.327): calcd. C 75.69, H 4.76, N 4.41; found C 75.79, H 4.81, N 4.44%.

2-(4-Chlorophenyl)-4-methoxy-5H-[1]benzopyrano[3,4-c]pyridin-5-one (2c): Using the general procedure **1b** (2.59 g; 10 mmol) and malononitrile (0.66 g; 10 mmol) in methanol (25 ml) gave **2c**. With a reaction time of 72h. Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 222–224 °C, yield 15%. IR: ν_{max} 1738 (C=O), 1592, 1547 cm⁻¹ (C=N, C=C). ^1H NMR (CDCl_3): δ 4.26 (s, 3H, OCH₃), 7.33–7.58 (m, 5H, arom. H), 7.91 (s, 1H, hetero. H-1), 8.07–8.13 (m, 3H, arom. H). MS: m/z (%) 339 [(M+2), 40], 337 [(M), 98], 322 (2), 308(49), 307 (19), 306 (5), 137 (100). Anal. for $\text{C}_{19}\text{H}_{12}\text{ClNO}_3$ (337.750): calcd. C 67.56, H 3.58, N 4.15; found C 67.65, H 3.65, N 4.19%.

2-(4-Chlorophenyl)-4-ethoxy-5H-[1]benzopyrano[3,4-c]pyridin-5-one (2d): Using the general procedure **1b** (2.59 g; 10 mmol) and malononitrile (0.66 g; 10 mmol) in ethanol (25 ml) gave **2d**. With a reaction time of 48h. Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (3:1 v/v) for elution, m.p. 208–210 °C, yield 14%. IR: ν_{max} 1734 (C=O), 1594, 1545 cm⁻¹ (C=N, C=C). ^1H NMR (CDCl_3): δ 1.51 (t, $J = 7.2$ Hz, 3H, CH₃), 4.69 (q, $J = 7.2$ Hz, 2H, OCH₂), 7.19–7.53 (m, 5H, arom. H), 7.84 (s, 1H, hetero. H-1), 8.02–8.05 (m, 3H, arom. H). MS: m/z (%) 353 [(M+2), 21], 351 [(M), 88], 336 (60), 323 (46), 322(18), 307(100), 306(8). Anal. for $\text{C}_{20}\text{H}_{14}\text{ClNO}_3$ (351.770): calcd. C 68.28, H 4.01, N 3.98; found C 68.24, H 3.98, N 4.00%.

4-Methoxy-2-(4-methylphenyl)-5H-[1]benzopyrano[3,4-c]pyridin-5-one (2e): Using the general procedure **1c** (2.38 g; 10 mmol) and malononitrile (0.66 g; 10 mmol) in methanol (25 ml) gave **2e**. With a reaction time of 72h. Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for

elution, m.p. 216–217 °C, yield 16%. IR: ν_{\max} 1740 (C=O), 1591, 1548 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 2.45 (s, 3H, CH_3), 4.28 (s, 3H, OCH_3), 7.32–7.57 (m, 5H, arom. H), 7.94 (s, 1H, hetero. H-1), 8.07–8.12 (m, 3H, arom. H). MS: m/z (%) 317 [(M), 100], 302 (2), 288 (51), 287 (14), 286 (6). Anal. for $\text{C}_{20}\text{H}_{15}\text{NO}_3$ (317.327): calcd. C 75.69, H 4.76, N 4.41; found C 75.69, H 4.78, N 4.47%.

4-Ethoxy-2-(4-methylphenyl)-5H-[1]benzopyrano[3,4-c]pyridin-5-one (2f): Using the general procedure **1c** (2.38 g; 10 mmol) and malononitrile (0.66 g; 10 mmol) in ethanol (25 ml) gave **2f**. With a reaction time of 72h. Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 156–158 °C, yield 15%. IR: ν_{\max} 1747 (C=O), 1591, 1546 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 1.57 (t, $J=7.2$ Hz, 3H, CH_2CH_3), 2.45 (s, 3H, CH_3), 4.77 (q, $J=7.2$ Hz, 2H, OCH_2), 7.31–7.56 (m, 5H, arom. H), 7.91 (s, 1H, hetero. H-1), 8.05–8.11 (m, 3H, arom. H). MS: m/z (%) 331 [(M), 89], 316 (75), 303 (56), 302 (15), 287 (100), 286 (16). Anal. for $\text{C}_{21}\text{H}_{17}\text{NO}_3$ (331.357): calcd. C 76.11, H 5.17, N 4.23; found C 76.16, H 5.22, N 4.20%.

4-Amino-2-methoxy-6-phenyl-3,5-pyridinedicarbonitrile (3a): Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 221–223 °C, yield 64%. IR: ν_{\max} 3341, 3244 (NH_2), 2222 (C≡N), 1660, 1563 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 4.11 (s, 3H, OCH_3), 5.68 (s, 2H, NH_2), 7.49–7.96 (m, 5H, arom. H). MS: m/z (%) 250 [(M), 51], 249 (27), 220 (10), 219 (15), 77 (100). Anal. for $\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}$ (250.250): calcd. C 67.19, H 4.03, N 22.39; found C 67.30, H 4.11, N 22.27%.

4-Amino-2-ethoxy-6-phenyl-3,5-pyridinedicarbonitrile (3b): Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 217–218 °C, yield 53%. IR: ν_{\max} 3452, 3328, 3235 (NH_2), 2231, 2216 (C≡N), 1651, 1568 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 1.44 (t, $J=6.9$ Hz, 3H, CH_3), 4.58 (q, $J=6.9$ Hz, 2H, OCH_2), 5.62 (s, 2H, NH_2), 7.48–7.94 (m, 5H, arom. H). MS: m/z (%) 264 [(M), 35], 263 (5), 249 (58), 236 (61), 220 (24), 219 (14), 77 (100). Anal. for $\text{C}_{15}\text{H}_{12}\text{N}_4\text{O}$ (264.280): calcd. C 68.17, H 4.58, N 21.20; found C 68.15, H 4.55, N 21.18%.

4-Amino-6-(4-chlorophenyl)-2-methoxy-3,5-pyridinedicarbonitrile (3c): Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 265–267 °C, yield 49%. IR: ν_{\max} 3367, 3243 (NH_2), 2229 (C≡N), 1680, 1564 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 4.11 (s, 3H, OCH_3), 5.62 (s, 2H, NH_2), 7.48 (d, $J=8.7$ Hz, 2H, arom. H), 7.90 (d, $J=8.7$ Hz, 2H, arom. H). MS: m/z (%) 286 [(M+2), 33], 284 [(M), 100], 283 (56), 254 (12), 253 (6). Anal. for $\text{C}_{14}\text{H}_9\text{ClN}_4\text{O}$ (284.695): calcd. C 59.06, H 3.19, N 19.68; found C 58.93, H 3.10, N 19.79%.

4-Amino-6-(4-chlorophenyl)-2-ethoxy-3,5-pyridinedicarbonitrile (3d): Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (3:1 v/v) for elution, m.p. 229–231 °C, yield 40%. IR: ν_{\max} 3385, 3341, 3245 (NH_2), 2228, 2210 (C≡N), 1661, 1558 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 1.38 (t, $J=7.2$ Hz, 3H, CH_3), 4.50 (q, $J=7.2$ Hz, 2H, OCH_2), 5.58 (s, 2H, NH_2), 7.41 (d, $J=8.7$ Hz, 2H, arom. H), 7.81 (d, $J=8.4$ Hz, 2H, arom. H). MS: m/z (%) 300 [(M+2), 28], 298 [(M), 85], 297 (6), 283 (97), 270 (100), 254 (31), 253 (3). Anal. for $\text{C}_{15}\text{H}_{11}\text{ClN}_4\text{O}$ (298.723): calcd. C 60.31, H 3.71, N 18.76; found C 60.36, H 3.77, N 18.78%.

4-Amino-2-methoxy-6-(4-methylphenyl)-3,5-pyridinedicarbonitrile (3e): Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 253–255 °C, yield 68%. IR: ν_{\max} 3406, 3347, 3252 (NH_2), 2223, 2210 (C≡N), 1658, 1570 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 2.43 (s, 3H, CH_3), 4.11 (s, 3H, OCH_3), 5.60 (s, 2H, NH_2), 7.31 (d, $J=8.1$ Hz, 2H, arom. H), 7.86 (d, $J=8.4$ Hz, 2H, arom. H). $^{13}\text{C NMR}$ ($\text{DMSO}-d_6$) "APT": δ 26.22 (CH_3), 59.87 (OCH_3), 81.24, 91.79 (hetero. C-5, C-3 respectively), 118.47, 120.76 (2 C≡N), 133.76, 133.97 (arom. CH), 139.08, 145.91, 164.49, 168.40, 170.87 (arom. quaternary C). MS: m/z (%) 264 [(M), 100], 263 (44), 234 (11), 233 (7). Anal. for $\text{C}_{15}\text{H}_{12}\text{N}_4\text{O}$ (264.280): calcd. C 68.17, H 4.58, N 21.20; found C 68.18, H 4.60, N 21.21%.

4-Amino-2-ethoxy-6-(4-methylphenyl)-3,5-pyridinedicarbonitrile (3f): Colourless crystals purified by silica gel TLC using chloroform-light petroleum (60–80 °C) (2:1 v/v) for elution, m.p. 225–227 °C, yield 65%. IR: ν_{\max} 3398, 3342, 3248 (NH_2), 2225, 2210 (C≡N), 1659, 1570 cm^{-1} (C=N, C=C). $^1\text{H NMR}$ (CDCl_3): δ 1.44 (t, $J=7.2$ Hz, 3H, CH_2CH_3), 2.43 (s, 3H, CH_3), 4.58 (q, $J=7.2$ Hz, 2H, OCH_2), 5.61 (s, 2H, NH_2), 7.30 (d, $J=8.1$ Hz, 2H, arom. H), 7.84 (d, $J=8.4$ Hz, 2H, arom. H). MS: m/z (%) 278 [(M), 100], 277 (8), 263 (99), 250 (94), 234 (31), 233 (7). Anal. for $\text{C}_{16}\text{H}_{14}\text{N}_4\text{O}$ (278.300): calcd. C 69.05, H 5.07, N 20.13; found C 69.00, H 5.03, N 20.19%.

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References

- J. Mirek, *Chem. Scr.* 1988, **28**, 295.
- A.M. Shestopalov, V.K. Promonenkov, Yu.A. Sharanin, L.A. Rodinovskaya and S.Yu. Sharanin, *Zh. Org. Khim.*, 1984, **20**, 1517.
- P. Victory, J.L. Borrell, A.V. Ferran, C. Seoane and J.L. Soto, *Tetrahedron Lett.*, 1991, **32**, 5375.
- S.K. El-Sadany, S.M. Sharaf, A.I. Darwish and A.A. Youssef, *Ind. J. Chem.*, 1991, **30**, 567.
- L.G. Bechert and H.H. Otto, *Arch. Pharm. (Weinheim)* 1991, **324**, 563.
- J.L. Soto, C. Seoane, N. Martin and L.A. Blanco, *Heterocycles*, 1983, **20**, 803.
- J.L. Soto, C. Seoane and J.A. Ciller, *An. Quim. Ser., C* 1980, **76**, 281; *Chem. Abstr.* 1981, **94**, 192085.
- N. Mishriky, F.M. Asaad, Y.A. Ibrahim and A.S. Girgis, *Recl. Trav. Chim. Pays-Bas*, 1994, **113**, 35.
- M.M. Al-Arab, H.D. Tabbat, B.S. Ghanem and M.M. Olmstead, *Synthesis* 1990, 1157.
- M.M. Al-Arab, *J. Heterocycl. Chem.*, 1989, **26**, 1665.
- D.V. Tyndall, T. Al-Nakib and M.J. Meegan, *Tetrahedron Lett.*, 1988, **29**, 2703.
- T. Al-Nakib, D.V. Tyndall and M.J. Meegan, *J. Chem. Res., (S)* 1988, 301.
- N. Mishriky, F.M. Asaad, Y.A. Ibrahim and A.S. Girgis, *J. Chem. Res., (S)* 1997, 316.
- N. Mishriky, Y.A. Ibrahim, A.S. Girgis and N.G. Fawzy, *Pharmazie* 2000, **55**, 269.
- A.S. Girgis and I.S. Ahmed-Farag, *Z. Naturforsch.*, 2003, **58b**, 698.
- F. De Vos, F. Dumont, P. Santens, G. Slegers, R.A. Dierckx and J. De Ruck, *J. Labelled Compd. Radiopharm.*, 2000, **43**, 989.
- D.T. Connor, S.R. Miller, P.C. Unangst and L.D. Wise, (Warner – Lambert Co., USA) U.S. US 5,760,050 (Cl. 514-291; A61K31/44), 2 Jun. 1998, *Chem. Abstr.*, 1998, **129**, 41081.
- P.C. Unangst, T. Capiris, D.T. Connor, T.G. Heffner, R.G. MacKenzie, S.R. Miller, T.A. Pugsley and L.D. Wise, *J. Med. Chem.*, 1997, **40**, 2688.
- D.T. Connor, P.C. Unangst, C.F. Schwender, R.J. Sorenson, M.E. Carethers, C. Puchalski, R.E. Brown and M.P. Finkel, *J. Med. Chem.*, 1989, **32**, 683.
- D.T. Connor, C.F. Schwender, R.J. Sorenson and P.C. Unangst, (Warner – Lambert Co.) U.S. US 4,404,138 (Cl. 260-244; C07D491/052) 13 Sep. 1983, *Chem. Abstr.*, 1984, **100**, 22655.
- D.T. Connor, C.F. Schwender, R.J. Sorenson and P.C. Unangst, (Warner – Lambert Co.) U.S. US 4,382,939 (Cl. 424-256; A61K31/455) 10 May 1983, *Chem. Abstr.*, 1983, **99**, 38446.
- R.E. Brown, C. Puchalski and J. Shavel, U.S. 4,117,140 (Cl. 424-267; C07D491/04) 26 Sep. 1978, *Chem. Abstr.*, 1979, **90**, 87429.
- R.E. Brown, C. Puchalski and J. Shavel, (Warner – Lambert Co.) Ger. Offen. 2,623,256 (Cl. C07D491/04) 30 Dec. 1976, *Chem. Abstr.*, 1977, **86**, 121317.
- R.E. Brown, C. Puchalski and J. Shavel, (Warner – Lambert Co.) U.S. 3,962,266 (Cl. 260-295T; C07D519/00) 8 Jun. 1976, *Chem. Abstr.* 1976, **85**, 160065.
- Full crystallographic details, excluding structure factors, have been deposited at Cambridge Crystallographic Data Centre (CCDC) as supplementary publication number CCDC 232212.
- A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M.C. Burla, G. Polidori and M. Camalli, *J. Appl. Crystallogn.*, 1994, **27**, 435.
- S. Mackay, C.J. Gilmore, C. Edwards, N. Stewart and K. Shankland (1999). maXus Computer Program for Solution and Refinement of Crystal Structures. Bruker Nonius. The Netherlands, MacScience, Japan & The University of Glasgow.
- (a) R.C. Elderfield and T.P. King, *J. Am. Chem. Soc.*, 1954, **76**, 5439; (b) K.S.R.K.M. Rao and N.V.S. Rao, *Ind. J. Chem.*, 1968, **6**, 66.