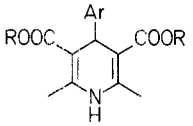
Synthesis of Dialkyl 2-(2-Hydroxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylates and Alkyl 2,4-Dimethyl-5-oxo-5*H*-[1]benzopyrano[4,3-*b*]-pyridine-3-carboxylates

C. N. O'Callaghan

Medical Research Council of Ireland Laboratories, Chemistry Building, Trinity College, Dublin 2, Ireland

The reaction of 2-hydroxybenzaldehydes with 3-oxobutanoic esters and excess ammonia in acetic acid at room temperature yields dialkyl 2-(2-hydroxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylates and their 2-(3,5-dialkoxycarbonyl-4,6-dimethyl-1,2,3-trihydropyridinium-2-yl)-phenoxide zwitterions. Mild oxidation of these compounds is accompanied by lactonisation, with formation of alkyl 2,4-dimethyl-5-oxo-5*H*-[1]benzopyrano[4,3-*b*]pyridine-3-carboxylates, which had previously been incorrectly formulated. Reaction of other *o*-substituted benzaldehydes with alkyl 3-aminocrotonates in acetic acid at room temperature also yields dialkyl 2-aryl-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylates, as well as the normal 1,4-dihydropyridine Hantzsch esters.

The widespread pharmacological use of 4-aryl-1,4-diydropyridine derivatives **1**[1] has emphasized the importance of the Hantzsch synthesis of these compounds from aryl aldehydes with ketoesters and ammonia.[2] It has recently been shown that, by modifying the experimental conditions, it is possible to obtain instead the isomeric 1,2-dihydropyridines **2** as the main products.[3]



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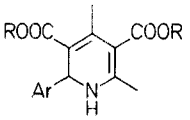

2

The failure of 2-hydroxybenzaldehydes to react with ketoesters to form „normal" Hantzsch-type 1,4-dihydropyridine diesters **1** has long been known,[4] but under the modified reaction conditions[3] 2-hydroxybenzaldehydes behave like other arenecarboxaldehydes, yielding the 1,2-dihydropyridines **6**. When excess ammonia is added to a mixture of salicylaldehyde (**3**, X = H) and methyl acetoacetate at room temperature, and the solution is then reacidified, the main products are the yellow 1,2-dihydropyridine **6a** and its colourless zwitterionic form **5a**.

The physical properties of the 1,2-dihydropyridines **6** resemble those of other 1,2-dihydropyridines **2**,[3] the ^{1}H-NMR spectra being characterised by a signal for 2-H which is coupled to NH. The zwitterionic forms **5** in solution change slowly into the hydroxycompounds **6**. (Only a zwitterion **5b** is obtained from the reaction of 2-hydroxy-3-methoxybenzaldehyde with methyl acetoacetate and ammonia, but recrystallisation from methanol converts this into **6b**).

Mild oxidation of the diester **6a** yields methyl 2,4-dimethyl-5-oxo-5*H*-[1]benzopyrano[4,3-*b*]pyridine-3-carboxylate (**7**, R = CH_3, X = H) (traces of which are obtained during the preparation of the diesters **5a** and **6a**); the same product is obtained by ring closure of dimethyl 2-(2-methoxyphenyl)-4,6-dimethylpyridine-3,5-dicarboxylate **(8)**. The reaction of salicylaldehyde (**3**, X = H) with methyl 3-aminocrotonate (methyl 3-amino-2-butenoate; **11**, R = CH_3) in acetic acid at room temperature also yields the same benzopyrano[4,3-*b*]pyridine derivative (**7**, R = CH_3, X = H); new compounds prepared by this latter method are listed in Table 3. This reaction presumably takes place via the intermediates **5a** and **6a** which are not isolated, but undergo oxidation and subsequent lactonisation on storing in acetic acid.

Compound **7**, R = CH_3, X = H, and some substituted derivatives of it have previously been prepared by similar routes, but have been formulated incorrectly as benzopyrano[3,4-*c*]pyridines **10**.[5,6] In fact, the compounds properly formulated as **10** are obtained by lactonisation of dimethyl 4-(2-methoxyphenyl)-2,6-dimethylpyridine-3,5-dicarboxylate **(9)**. They are also obtained by mild oxidation of the 3,10b-dihydrobenzopyrano-[3,4-*c*]pyr-

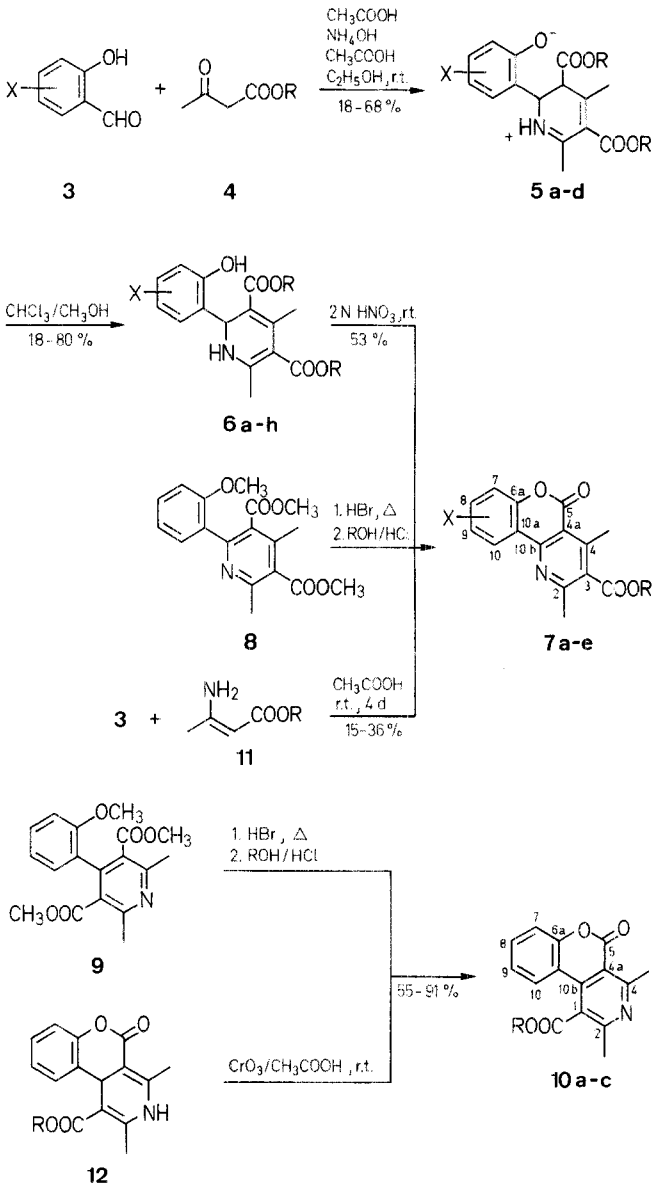

Table 1. 2-(3,5-Dimethoxycarbonyl-4,6-dimethyl-1,2,3-trihydropyridinium-2-yl)-phenoxides **(5)** Prepared

Product	R	X	Yield[a] (%)	m.p. (°C) (solvent)	Molecular Formula[b]	IR (Nujol) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$) δ(ppm)
5a	CH_3	H	55	145–148 (benzene)	$C_{17}H_{19}NO_5$ (317.3)	3305, 1748, 1650, 1585w	1.92 (s, 3H, CH_3); 2.09 (s, 3H, CH_3); 3.01 (d, 1H, 3′-H); 3.71 (s, 3H, OCH_3); 3.73 (s, 3H, OCH_3); 4.55 (dd, 1H, 2′-H); 4.84 (br. s, 1H, NH); 6.77–7.20 (m, 4H$_{arom}$)
5b	CH_3	3-OCH_3	50	141–143 (benzene)	$C_{18}H_{21}NO_6$ (347.4)	3305, 1750, 1652, 1587w	1.97 (s, 3H, CH_3); 2.09 (s, 3H, CH_3); 3.01 (d, 1H, 3′-H); 3.70 (s, 3H, OCH_3); 3.72 (s, 3H, OCH_3); 3.85 (s, 3H, OCH_3); 4.55 (dd, 1H, 2′-H); 4.96 (br. s, 1H, NH); 6.61–6.92 (m, 3H$_{arom}$)
5i	CH_3	5-OCH_3	68	133–136 (ether)	$C_{18}H_{21}NO_6$ (347.4)	3305, 1745, 1652, 1565	1.89 (s, 3H, CH_3); 2.08 (s, 3H, CH_3); 2.95 (d, 1H, 3′-H); 3.70 (s, 3H, OCH_3); 3.72 (s, 3H, OCH_3); 3.74 (s, 3H, OCH_3); 4.49 (dd, 1H, 2′-H); 4.93 (br. s, 1H, NH); 6.62–6.81 (m, 3H$_{arom}$)
5j	CH_3	5-Cl	18	163–166 (ether)	$C_{17}H_{18}ClNO_5$ (351.8)	3325, 1745, 1652, 1555	1.70 (s, 3H, CH_3); 1.98 (s, 3H, CH_3); 2.83 (d, 1H, 3′-H); 3.60 (s, 3H, OCH_3); 3.63 (s, 3H, OCH_3); 4.28 (dd, 1H, 2′-H); 4.44 (br. s, 1H, NH); 6.67–7.38 (m, 3H$_{arom}$)

[a] Optimised yield.
[b] Satisfactory microanalyses obtained: C ±0.3, H ±0.17, N ±0.15.

idines **12**, the structure of which is established unequivocally by their ^{1}H-NMR spectra.

The reaction of 2-hydroxybenzaldehydes with alkyl 3-aminocrotonates to yield benzopyrano[4,3-*b*]pyridines **7** (derived from 1,2-dihydropyridines) rather than benzopyrano[3,4-*c*]pyridines **10** (derived from 1,4-dihydropyridines) appears to run counter to the finding, long known[7] and reported,[2] that the reaction of other aromatic aldehydes with 3-aminocrotonates in acetic acid yields „normal" symmetrical Hantzsch-type 1,4-dihydropyridine derivatives. However, the experimental conditions employed in the past (e.g., heating the reactants in acetic acid solution under reflux overnight[8]) destroy any 1,2-dihydropyridines which may be formed (and which are relatively unstable), leaving 1,4-dihydropyridines as the only stable, isolable products. A limited investigation shows that at room temperature the reaction of *o*-substituted benzaldehydes with methyl 3-aminocrotonate in acetic acid yields a mixture of 1,2-dihydropyridines **2** (mainly) and 1,4-dihydropyridines **1**.

Dialkyl 2-(2-hydroxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylates (6) and 2-(3,5-Dialkoxycarbonyl-4,6-dimethyl-1,2,3-trihydropyridinium-2-yl)-phenoxides (5); General Procedure:

To a solution of the 2-hydroxybenzaldehyde (10 mmol) and an alkyl 3-oxobutanoate (**4**; 20 mmol) in acetic acid (2 ml) at room temperature is added ammonia solution (33%; 4.4 ml), followed by acetic acid (2 ml) and ethanol (6 ml). On storing the mixture overnight at room temperature, a heavy oil separates. As soon as signs of crystallisation or solidification appear (which normally occurs after 1 day, but 2 or 3 days may be necessary), the aqueous upper layer is decanted and discarded. The partly solid residue is air-dried for 3 days, and full crystallisation is generally achieved by addition of a little ether and scratching. When it is clear from the IR spectra of the crude product that a mixture of the two compounds **5** and **6** is present, extraction with benzene (2 × 40 ml) removes the zwitterionic compound **5**, leaving undissolved the dihydropyridine **6**; both products are then purified by further recrystallization, using minimal amounts of solvent.

Alkyl 2,4-Dimethyl-5-oxo-5*H*-[1]benzopyrano[4,3-b]pyridine-3-carboxylates (7); General or Typical Procedures:

Method A, from Dihydropyridines **6**:

Methyl 2,4-Dimethyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carb-

Table 2. Dialkyl 2-(2-Hydroxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylates **(6)** Prepared

Product	R	X	Yield[a] (%)	m.p. (°C) (solvent)	Molecular Formula[b]	IR (Nujol) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$) δ(ppm)
6a	CH_3	H	18	167–170 (methanol)	$C_{17}H_{19}NO_5$ (317.3)	3390w, 3300, 1700, 1665, 1595	2.18 (s, 3H, CH_3); 2.36 (s, 3H, CH_3); 3.69 (s, 6H, $2OCH_3$); 5.61 (br. s, 1H, NH); 5.81 (d, 1H, 2-H); 6.72–7.23 (m, 5H, $4H_{arom}$, 1OH)
6b	CH_3	3-OCH_3	80[c]	156–159	$C_{18}H_{21}NO_6$ (347.4)	3395w, 3290, 1695, 1660, 1600	2.13 (s, 3H, CH_3); 2.46 (s, 3H, CH_3); 3.62 (s, 3H, OCH_3); 3.67 (s, 3H, OCH_3); 3.87 (s, 3H, OCH_3); 5.91 (br. s, 3H: NH, 2-H, OH); 6.77 (s, $3H_{arom}$)
6c	CH_3	4-OCH_3	28	167–170 (methanol)	$C_{18}H_{21}NO_6$ (347.4)	3360, 3290, 1705, 1645, 1595	2.18 (s, 3H, CH_3); 2.31 (s, 3H, CH_3); 3.68 (s, 9H, $3OCH_3$); 5.38 (br. s, 1H, NH); 5.66 (d, 1H, 2-H); 6.35–7.21 (m, $3H_{arom}$); 7.56 (s, 1H, OH)
6d	CH_3	3-OC_2H_5	37	107–109 (methanol)	$C_{19}H_{23}NO_6$ (361.4)	3380br, 1710, 1655, 1590, 1550	1.43 (t, 3H, OCH_2CH_3); 2.13 (s, 3H, CH_3); 2.43 (s, 3H, CH_3); 3.62 (s, 3H, OCH_3); 3.74 (s, 3H, OCH_3); 4.10 (q, 2H, OCH_2CH_3); 5.92 (br. s, 2H, NH, 2-H); 6.75 (br. s, 4H, $3H_{arom}$, 1OH)
6e	C_2H_5	H	32	97–100 (methanol)	$C_{19}H_{23}NO_5$, H_2O[d] (363.4)	3520br, 3300br, 1690, 1650, 1590	1.14 (t, 3H, OCH_2CH_3); 1.19 (t, 3H, OCH_2CH_3); 1.57 (s, 2H, H_2O); 2.10 (s, 3H, CH_3); 2.29 (s, 3H, CH_3); 4.04 (q, 2H, OCH_2CH_3); 4.13 (q, 2H, OCH_2CH_3); 5.69 (br. s, 1H, NH); 5.75 (d, 1H, 2-H); 6.64–7.03 (m, $4H_{arom}$); 7.33 (br. s, 1H, OH)
6f	C_2H_5	3-OCH_3	28	103–105 (PE)[e]	$C_{20}H_{25}NO_6$ (375.4)	3390, 1687, 1660, 1590	1.17 (t, 3H, OCH_2CH_3); 1.28 (t, 3H, OCH_2CH_3); 2.14 (s, 3H, CH_3); 2.47 (s, 3H, CH_3); 3.88 (s, 3H, OCH_3); 4.16 (q, 2H, OCH_2CH_3); 4.21 (q, 2H, OCH_2CH_3); 5.84 (br. s, 1H, NH); 5.94 (d, 1H, 2-H); 6.78 (s, 4H, 3-H_{arom}, 1OH)
6g	C_2H_5	4-OCH_3	57	155–108 (methanol)	$C_{20}H_{25}NO_6$ (375.4)	3340, 1698, 1633, 1580w	1.23 (t, 3H, OCH_2CH_3); 1.32 (t, 3H, OCH_2CH_3); 2.19 (s, 3H, CH_3); 2.34 (s, 3H, CH_3); 3.68 (s, 3H, OCH_3); 4.13 (q, 2H, OCH_2CH_3); 4.22 (q, 2H, OCH_2CH_3); 5.58 (br. s, 1H, NH); 5.72 (d, 1H, 2-H); 6.30–7.22 (m, $3H_{arom}$); 7.86 (s, 1H, OH)
6h	C_2H_5	3-OC_2H_5	24	106–109	$C_{21}H_{27}NO_6$ (389.45)	3380, 3320w, 1695, 1675, 1605	1.28 (t, 3H, OCH_2CH_3); 1.37 (t, 3H, OCH_2CH_3); 1.44 (t, 3H, OCH_2CH_3); 2.14 (s, 3H, CH_3); 2.47 (s, 3H, CH_3); 4.06 (q, 2H, OCH_2CH_3); 4.15 (q, 2H, OCH_2CH_3); 4.19 (q, 2H, OCH_2CH_3); 5.84 (br. s, 2H, NH, OH); 5.94 (d, 1H, 2-H); 6.73 (s, $3H_{arom}$)

[a] Optimised yield.
[b] Satisfactory microanalyses obtained: C ± 0.2, H ± 0.19, N ± 0.18.
[c] Obtained from the corresponding zwitterion **5b**.
[d] Retains 1 H_2O tenaciously.
[e] Petroleum ether b.p. 60–80°.

Table 3. Ethyl 2,4-Dimethyl-5-oxo-5H-[1]benzopyrano[4,3-*b*]pyridine-3-carboxylates (**7**) Prepared

Product	R	X	Yield[a] (%)	m.p. (°C) (solvent)	Molecular Formula[b]	IR (Nujol) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$) δ (ppm)
7e[c]	C_2H_5	H	24	112–113 (methanol)	$C_{17}H_{15}NO_4$ (297.3)	1740, 1720[d], 1615, 1600, 1560	1.42 (t, 3H, OCH_2CH_3); 2.67 (s, 3H, CH_3); 2.79 (s, 3H, CH_3); 4.47 (q, 2H, OCH_2CH_3); 7.24–7.57 (m, 3H$_{arom}$); 8.60 (dd, 1H$_{arom}$)
7g	C_2H_5	8-OCH_3	22	135–136 (methanol)	$C_{18}H_{17}NO_4$ (311.3)	1735, 1725[d], 1618, 1598, 1565	1.42 (t, 3H, OCH_2CH_3); 2.64 (s, 3H, CH_3); 2.77 (s, 3H, CH_3); 3.90 (s, 3H, OCH_3); 4.47 (q, 2H, OCH_2CH_3); 6.77–6.93 (m, 2H$_{arom}$); 8.46 (d, 1H$_{arom}$)
7k	C_2H_5	9-OCH_3	30	169–171 (methanol)	$C_{18}H_{17}NO_4$ (311.3)	1735, 1720[d], 1610w, 1570	1.43 (t, 3H, OCH_2CH_3); 2.68 (s, 3H, CH_3); 2.79 (s, 3H, CH_3); 3.92 (s, 3H, OCH_3); 4.48 (q, 2H, OCH_2CH_3); 7.02–7.32 (m, 2H$_{arom}$); 8.03 (d, 1H$_{arom}$)
7j	C_2H_5	9-Cl	36	181–182 (methanol)	$C_{17}H_{14}ClNO_4$ (331.65)	1745, 1735[d], 1600w, 1570	1.43 (t, 3H, OCH_2CH_3); 2.67 (3H, s, CH_3); 2.79 (3H, s, CH_3); 4.48 (q, 2H, OCH_2CH_3); 7.19–7.57 (m, 2H$_{arom}$); 8.03 (d, 1H$_{arom}$)
7h	C_2H_5	7-OC_2H_5	15	125–127 (methanol)	$C_{19}H_{19}NO_5$ (341.35)	1740, 1725[d], 1620, 1600w, 1560	1.43 (t, 3H, OCH_2CH_3); 1.52 (t, 3H, OCH_2CH_3); 2.67 (s, 3H, CH_3); 2.81 (s, 3H, CH_3); 4.18 (q, 2H, OCH_2CH_3); 4.48 (q, 2H, OCH_2CH_3); 7.02–7.36 (m, 2H$_{arom}$); 8.17 (dd, 1H$_{arom}$)

[a] Optimised yield.
[b] Satisfactory microanalyses obtained: C ±0.3, H ±0.22, N ±0.13.
[c] ^{13}C-NMR (DMSO-d_6): δ = 167.1 (ester C=O); 159.5 (C-2); 158.9 (C-5); 152.0 (C-6a); 151.3 (C-10b); 148.8 (C-4); 132.4 (C-8); 131.0 (C-3); 124.7 (C-10); 124.3 (C-9); 118.2[e] (C-4a); 116.2 (C-7); 113.4[e] (C-10a); 61.7 (OCH_2); 23.1 (2-CH_3); 18.4 (4-CH_3); 13.7 ppm (OCH_2CH_3).
[d] The lactone and ester bands were only partially resolved.
[e] These assignments may be interchanged.

Table 4. Benzopyrano[3,4-*c*]pyridine Derivatives Prepared

Product	R	Yield[a] (%)	m.p. (°C) (solvent)	Molecular Formula[a]	IR (Nujol) ν (cm^{-1})	^{1}H-NMR δ (ppm)
12a	CH_3	8	242–245 (methanol)	$C_{16}H_{15}NO_4$ (285.3)	3285, 1715, 1705, 1640, 1620	(DMSO-d_6) 2.01 (s, 3H, CH_3); 2.25 (s, 3H, CH_3); 3.59 (s, 3H, OCH_3); 4.74 (s, 1H, 10b-H); 6.70–7.51 (m, 4H$_{arom}$); 8.90 (s, 1H, NH)
12b	C_2H_5	12	229–232 (methanol)	$C_{17}H_{17}NO_4$ (299.3)	3295, 1720, 1700, 1645, 1625	(DMSO-d_6) 1.10 (t, 3H, OCH_2CH_3); 2.01 (s, 3H, CH_3); 2.25 (s, 3H, CH_3); 4.10 (q, 2H, OCH_2CH_3); 4.74 (s, 1H, 10b-H); 6.72–7.19 (m, 4H$_{arom}$); 8.83 (s, 1H, NH)
10a	CH_3	87[d]	148–150 (methanol)	$C_{16}H_{13}NO_4$ (283.3)	1750, 1720[e], 1605, 1590, 1555	($CDCl_3$) 2.64 (s, 3H, CH_3); 3.06 (s, 3H, CH_3); 4.00 (s, 3H, OCH_3); 7.22–7.77 (m, 4H$_{arom}$)
10b[c]	C_2H_5	91[d]	134–136 (methanol)	$C_{17}H_{15}NO_4$ (297.3)	1750, 1720[e], 1608, 1592, 1556	($CDCl_3$) 1.39 (t, 3H, OCH_2CH_3); 2.65 (s, 3H, CH_3); 3.06 (s, 3H, CH_3); 4.49 (q, 2H, OCH_2CH_3); 7.23–7.88 (m, 4H$_{arom}$)
10c	H	55	244–246 (methanol)	$C_{15}H_{11}NO_4$ (269.25)	1735, 1720w, 1605w, 1590w, 1578	(DMSO-d_6) 2.60 (s, 3H, CH_3); 2.93 (s, 3H, CH_3); 5.12 (br. s, 1H, COOH); 7.29–8.19 (m, 4H$_{arom}$)

[a] Optimised yield.
[b] Satisfactory microanalyses obtained: C ±0.2, H ±0.09, N ±0.18.
[c] The lactone and ester bands were only partially resolved.
[d] Obtained by oxidation of the dihydrocompounds **12**.
[e] ^{13}C-NMR (DMSO-d_6) δ = 168.5 (ester C=O); 163.2 (C-4); 158.4 (C-2); 158.2 (C-5); 151.9 (C-6a); 138.7 (C-10b); 132.9 (C-8); 125.2 (C-10); 124.4 (C-9); 121.3 (C-1); 117.5 (C-7); 114.7[f] (C-4a); 112.9[f] (C-10a); 62.3 (OCH_2); 26.5 (4-CH_3); 22.5 (2-CH_3); 13.4 ppm (OCH_2CH_3).
[f] These assignments may be interchanged.

oxylate (**7**, R = CH_3, X = H): Dimethyl 2-(2-hydroxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**6a**; 100 mg, 0.315 mmol) is suspended in 2 normal nitric acid (10 ml) and this suspension is stirred at room temperature overnight. The product which separates is isolated by filtration and recrystallized twice from methanol; yield: 47 mg (53%); m.p. 151–153 °C (Lit.[5] m.p. 151–153 °C).

Method B, from Pyridine Derivative **8**:

2,4-Dimethyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylic Acid (**7**, R = X = H): Dimethyl 2-(2-methoxyphenyl)-4,6-dimethylpyridine-3,5-dicarboxylate[3] (**8**; 659 mg, 2 mmol; obtained by oxidation of the corresponding 1,2-dihydropyridine) is heated in boiling 48% hydrobromic acid (6 ml) for 1 h. The mixture is then cooled and poured onto ice (~ 100 g). The crude carboxylic acid is isolated by filtration and recrystallized from methanol; yield: 296 mg (55%); m.p. 217–218 °C.

$C_{15}H_{11}NO_4$ (269.3)	calc.	C 66.91	H 4.12	N 5.20
	found	66.71	4.11	5.32

IR (Nujol): ν = 1740, 1700, 1615w, 1600w, 1556, 1540 cm^{-1}.

^{1}H-NMR (DMSO-d_6): δ = 2.64 (s, 3H, CH_3); 2.71 (s, 3H, CH_3); 3.44 (br. s, 1H, COOH); 7.30–7.76 (m, 3H$_{arom}$); 8.43 ppm (dd, 1H$_{arom}$).

Methyl or Ethyl 2,4-Dimethyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylate (**7**, R = CH_3 or C_2H_5, X = H): Dry hydrogen chloride is passed through a solution of the carboxylic acid (**7**, R = X = H; 269 mg, 1 mmol) in methanol (75 ml) or ethanol (75 ml) for 15 min. The solution is then heated to reflux for 1 h, concentrated to 10 ml and the product **7** is isolated by filtration and purified by washing with water and recrystallisation from methanol.

Methyl Ester **7**, R = CH_3, X = H; yield: 128 mg (45%); m.p. 151–153°C (Lit.[5] m.p. 151–153°C).

Ethyl Ester **7e**, R = C_2H_5, X = H; yield: 166 mg (56%); m.p. 112–113°C.

Method C, from 2-Hydroxybenzaldehydes (**3**) and Alkyl 3-Amino-2-butenoates (**11**):

Alkyl 2,4-Dimethyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylates (**7a–e**; see Table 3): A solution of the 2-hydroxybenzaldehyde **3** (10 mmol) and ethyl 3-amino-2-butenoate (**11**, R = C_2H_5; 20 mmol) in acetic acid (10 ml) is stored at room temperature for 4 days. The crystalline ethyl 2,4-dimethyl-5-oxo-5*H*-[1]benzopyrano[4,3-b]pyridine-3-carboxylate (**7a–e**) which separates is collected by filtration and recrystallised from methanol.

Alkyl 2,4-Dimethyl-5-oxo-5*H*-[1]benzopyrano[3,4-*c*]pyridine-1-carboxylates (10a, b, c); General Procedures:

Method B, from Pyridine Derivative **9**:

Dimethyl 4-(2-Methoxyphenyl)-2,6-dimethylpyridine-3,5-dicarboxylate (**9**): A solution of chromium (VI) oxide (150 mg) in water (0.5 ml) is added to a stirred solution of dimethyl 4-(2-methoxyphenyl)2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate[9] (**1**, Ar = *o*-OCH_3-C_6H_4, R = CH_3; 663 mg, 2 mmol) in acetic acid (6 ml) and stirring is continued for 1 h at room temperature. The solution is then made basic with aqueous ammonia and the pyridine **9** which separates is isolated by suction and recrystallized from methanol; yield: 626 mg (95%); m.p. 80–81°C.

$C_{18}H_{19}NO_5$	calc.	C 65.6	H 5.81	N 4.25
(329.3)	found	65.4	5.72	4.06

IR (Nujol): ν = 1735, 1595 cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ = 2.61 (s, 6H, 2 CH_3); 3.51 (s, 6H, 2 OCH_3); 3.73 (s, 3H, OCH_3); 6.94–7.26 ppm (m, 4 H_{arom}).

2,4-Dimethyl-5-oxo-5 H-[1]benzopyrano[3,4-c]pyridine-1-carboxylic Acid (**10**, R = H): Diester **9** (659 mg, 2 mmol) is heated n boiling 48% hydrobromic acid (5 ml) for 1 h. The mixture is then cooled and poured onto ice (~ 100 g). The crude carboxylic acid is isolated by filtration and recrystallized from methanol; yield: 288 mg (53%); m.p. 244–246°C.

$C_{15}H_{11}NO_4$	calc.	C 66.9	H 4.12	N 5.20
(269.25)	found	66.8	4.02	5.38

Methyl or Ethyl 2,4-Dimethyl-5-oxo-5H-[1]benzopyrano[3,4-c]pyridine-1-carboxylate (**10a** or **10b**): Dry hydrogen chloride is passed through a solution of the carboxylic acid (**10**, R = H; 269 mg, 1 mmol) in methanol (25 ml) or ethanol (25 ml) for 15 min. The solution is then heated to reflux for 1 h, concentrated to 10 ml and the product is isolated by filtration and recrystallized from methanol. See Table 4.

Method D, via 3,10b-Dihydro Derivatives **12**:

Alkyl 2,4-Dimethyl-5-oxo-3,10b-dihydro-5H-[1]benzopyrano[3,4-c]pyridine-1-carboxylates (**12**): 2-Hydroxybenzaldehyde (1.221 g, 10 mmol) and methyl or ethyl acetoacetate (20 mmol) are added to a mixture of acetic acid (8 ml) and aqueous 33% ammonia solution (11.0 ml); ethanol (6 ml) and acetic acid (8 ml) are then added, and the solution heated on a water bath for 1.25 h. The ester **12** is collected from the hot solution by filtration, and recrystallised from methanol. See Table 4.

Alkyl 2,4-Dimethyl-5-oxo-5H-[1]benzopyrano[3,4-c]pyridine-1-carboxylates (**10**): The dihydro derivative **12** (100 mg) is dissolved in acetic acid (2 ml), a solution of chromium (VI) oxide (50 mg) in water (0.1 ml) is added, and the mixture is stirred for 1 h at room temperature. Addition of excess conc. ammonia solution (~ 4 ml) then releases the oxidised product **10** which is collected and recrystallised from methanol. See Table 4.

Reaction of 2-Methoxybenzaldehyde with Methyl 3-Amino-2-butenoate: A solution of 2-methoxybenzaldehyde (1.362 g, 10 mmol) and methyl 3-amino-2-butenoate (**4**; R = CH_3; 2.323 g, 20 mmol) in acetic acid (4 ml) is stored at room temperature for 1 day. The mixture of solid products which separates is collected by filtration and dried. Extraction of the solid with ether removes *dimethyl 2-(2-methoxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate* (**2**; R = CH_3, Ar = 2-OCH_3-C_6H_4) which is recovered from ether; yield: 1.193 g (36%); m.p. 150–152°C (Lit.[3] m.p. 150–152°C). The ether-insoluble residue is recrystallized from methanol to give *dimethyl 4-(2-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate* (**1**; R = CH_3, Ar = 2-OCH_3-C_6H_4); yield: 298 mg (9%); m.p. 202–203°C (Lit.[9] m.p. 205–206°C).

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