A Convenient, One-Step Synthesis of Methyl 2,4-Dimethyl-5-oxo-5*H*-[1]benzopyrano[3,4-c]pyridine-1-carboxylates

C. N. O'Callaghan

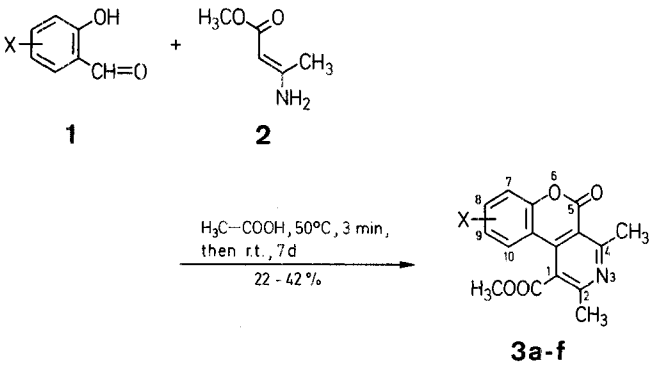
Medical Research Council of Ireland Laboratories, Chemistry Building, Trinity College, Dublin 2, Ireland

The reaction of *o*-hydroxybenzaldehydes with methyl 3-aminocrotonate in acetic acid at room temperature yields methyl 2,4-dimethyl-5-oxo-5*H*-[1]benzopyrano[3,4-*c*]pyridine-1-carboxylates, in 22–42% yield.

The preparation and biological properties of coumarins with 3:4-fused ring systems have recently been reviewed[1]; various methods are available for the preparation of benzopyrano[3,4-*c*]pyridine-5-ones[2–7], and the potential of compounds of this type as synthetic intermediates has recently been demonstrated[8]. Few ester derivatives of the system are known, however, although their biological significance has been recognized[9].

Ethyl 2,4-dimethyl-9-nitro-5-oxo-5*H*-[1]benzopyrano[3,4-*c*]pyridine-1-carboxylate has been prepared by a multi-step synthesis involving hydrolysis of the appropriate nitrile[9], but this method was not applicable to non-nitrated compounds. Two other ethyl esters were obtained in 7–10% yields as by-products from the reaction of ethyl acetoacetate with substituted *o*-hydroxybenzaldehydes in the presence of ammonium acetate[10]; the suggested synthesis of these compounds from 3-acetylcoumarin derivatives with methyl 3-aminocrotonate is not feasible, however, the 3-acetylcoumarin being recovered unchanged.

A simple, convenient synthesis of methyl 2,4-dimethyl-5-oxo-5*H*-[1]benzopyrano[3,4-*c*]pyridine-1-carboxylates **(3)** is provided by the reaction of *o*-hydroxybenzaldehydes **(1)** with methyl 3-aminocrotonate **(2)** in a 1:2 molar ratio, in acetic acid. Reaction conditions are mild, and any traces of minor contaminants are readily removable by recrystallization.



Methyl 2,4-Dimethyl-5-oxo-5*H*-[1]benzopyrano[3,4-*c*]pyridine-1-carboxylates (3); General Procedure:

The *o*-hydroxybenzaldehyde **1** (10 mmol) and methyl 3-aminocrotonate (**2**; 20 mmol) in glacial acetic acid (10 ml) are stirred at 50 °C for 3 min and then stored at room temperature for 7 days. The resultant crystalline precipitate is collected by filtration, washed with ethanol, and recrystallised.

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Table. Methyl 2,4-Dimethyl-5-oxo-5*H*-[1]benzopyrano[3,4-*c*]pyridine-1-carboxylates prepared

Product	X	Yield[a] [%]	m.p. [°C] (solvent)	Molecular Formula[b]	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6/TMS$_{int}$) δ [ppm]
3a	H	22	151–153[c] (methanol)	$C_{16}H_{13}NO_4$ (283.3)	1733, 1720[c], 1610, 1597	2.59 (s, 3H, CH_3); 2.66 (s, 3H, CH_3); 3.98 (s, 3H, OCH_3); 7.30–7.81 (m, 3H$_{arom}$); 8.48 (dd, 1H$_{arom}$)
3b	7-OCH_3	39	216–218[c] (ethanol)	$C_{17}H_{15}NO_5$ (313.3)	1732, 1723[c], 1610, 1597	2.59 (s, 3H, CH_3); 2.66 (s, 3H, CH_3); 3.93 (3,3H, OCH_3); 3.97 (s, 3H, OCH_3); 7.31–7.37 (m, 2H$_{arom}$); 7.93–8.21 (m, 1H$_{arom}$)
3c	8-OCH_3	34	174–176[c] (ethanol)	$C_{17}H_{15}NO_5$ (313.3)	1735, 1721[c], 1625, 1597	2.58 (s, 3H, CH_3); 2.66 (s, 3H, CH_3); 3.88 (s, 3H, OCH_3); 3.98 (s, 3H, OCH_3); 7.21–7.36 (m, 2H$_{arom}$); 8.25–8.42 (m, 1H$_{arom}$)
3d	9-OCH_3	26	193–195[c] (ethanol)	$C_{17}H_{15}NO_5$ (313.3)	1730, 1720[c], 1611	2.62 (s, 3H, CH_3); 2.69 (s, 3H, CH_3); 3.88 (s, 3H, OCH_3); 3.98 (s, 3H, OCH_3); 7.10–7.36 (m, 2H$_{arom}$); 7.86–7.96 (m, 1H$_{arom}$)
3e	7-OC_2H_5	32	186–188[c] (ethanol)	$C_{18}H_{17}NO_5$ (327.3)	1735, 1722[c], 1612 (w), 1594 (w)	1.39 (t, 3H, CH_3); 2.57 (s, 3H, CH_3); 2.67 (s, 3H, CH_3); 3.96 (s, 3H, OCH_3); 4.19 (q, 2H, OCH_2CH_3); 7.14–7.39 (m, 2H$_{arom}$); 7.92–8.13 (m, 1H$_{arom}$)
3f	9-Cl	42	205–206[c] (benzene)	$C_{16}H_{16}ClNO_4$ (317.7)	1740, 1724[c], 1614 (w), 1594	2.61 (s, 3H, CH_3); 2.68 (s, 3H, CH_3); 3.97 (s, 3H, OCH_3); 7.31–7.70 (m, 2H$_{arom}$); 8.38 (d, 1H$_{arom}$)

[a] Optimised yield.
[b] The microanalyses were in satisfactory agreement with the calculated values: C ±0.2, H ±0.19, N ±0.27; microanalyses were obtained by May & Baker Ltd. (Dagenham), England.
[c] The lactone and ester bands were only partially resolved.