## A Ready Synthesis of 4-Oxo-4*H*-pyrrolo[3,2,1-*ij*]quinolines

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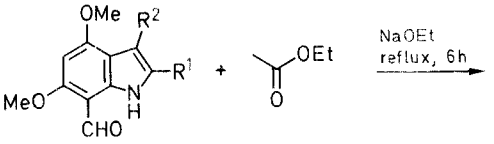
4,6-Dimethoxy-7-formylindoles undergo condensation with ethyl acetate in the presence of sodium ethoxide to yield new 4-oxo-4*H*-pyrrolo[3,2,1-*ij*]quinolines.

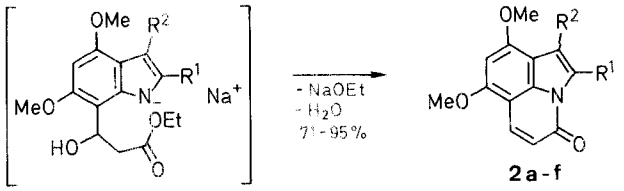
Pyrroloquinolines and their derivatives have received considerable attention because of their biological interest. Although 5-oxopyrrolo[3,2,1-*ij*]quinolines are known, information regarding the related 4-oxopyrroloquinoline system is rather scarce. Modified forms of the 4-oxopyrroloquinoline ring system are found in hippadine,[1] pratorinine,[2] and pratorimine[3] alkaloids recently isolated from the *Amaryllidaceae* family. 6-Oxopyrroloquinolines[4–7] are normally prepared by cyanoethylation of the indole nitrogen, followed by hydrolysis of cyano to carboxyl and cyclization with polyphosphoric acid. An isolated report describes the synthesis of 6-methyl-4-oxo-4*H*-pyrrolo[3,2,1-*ij*]quinoline[8] by the cyclization of 1-acetoacetylindole using forcing conditions.

Our previous use of 4,6-dimethoxyindoles[9] has enabled 7-substitution to be achieved readily. Thus Vilsmeier formylation leads to the 7-formylindoles **1**,[11] which have already been converted into a range of useful 7-substituted indoles.[10–11] We now report that the 7-formylindoles **1** undergo smooth reaction with ethyl acetate in the presence of sodium ethoxide to give the 4-oxopyrroloquinolines **2** directly in high yields (Table).

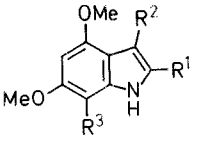
The ease of cyclization is significant as the presumed intermediate **3** was not isolated. However, in certain cases a trace amount of the α,β-unsaturated ester **4** was detected but also was not isolated. Presumably cyclization is assisted by the buttressing effect of the 6-methoxy group and consequent relief of steric hindrance.




**1a-f**




**2a-f**




**3** $R^3$ = $CH(OH)CH_2CO_2Et$
**4** $R^3$ = $CH{=}CHCO_2Et$

| 1–4 | $R^1$ | $R^2$ | 1–4 | $R^1$ | $R^2$ |
|---|---|---|---|---|---|
| **a** | H | H | **d** | 4-$BrC_6H_4$ | H |
| **b** | Ph | Ph | **e** | H | $CH_3$ |
| **c** | Ph | H | **f** | $-(CH_2)_4-$ | |

**Table.** 7,9-Dimethoxy-4-oxo-4*H*-pyrrolo[3,2,1-*ij*]quinolines **2** Prepared

| Product | Yield (%)[a] | mp (°C)[b] | Molecular Formula[c] | IR (Nujol)[d] ν (C=O) ($cm^{-1}$) | $^1$H-NMR ($CDCl_3$)[e] δ, J(Hz) | MS (70 eV)[f] m/z (%) |
|---|---|---|---|---|---|---|
| **2a** | 89 | 197–198 | $C_{13}H_{11}NO_3$ (229.2) | 1676 | 3.99, 4.09 (2s, 3H each, $OCH_3$); 6.34 (s, $1H_{arom}$); 6.46 (d, 1H, $J$ = 9.4); 6.90 (d, 1H, $J$ = 3.6); 7.78 (d, 1H, $J$ = 3.6); 7.98 (d, 1H, $J$ = 9.4) | 229 ($M^+$, 100); 214 (60); 188 (55); 171 (28) |
| **2b** | 74 | 246–247 | $C_{25}H_{19}NO_3$ (381.4) | 1678 | 3.84, 4.03 (2s, 3H each, $OCH_3$); 6.40 (s, $1H_{arom}$); 6.40 (d, 1H, $J$ = 9.5); 7.21–7.35 (m, $10H_{arom}$); 7.99 (d, 1H, $J$ = 9.5) | 381 ($M^+$, 100); 380 (39); 366 (28) |
| **2c** | 71 | 216–217 | $C_{19}H_{15}NO_3$ (305.3) | 1674 | 3.97, 4.03 (2s, 3H each, $OCH_3$); 6.39 (s, $1H_{arom}$); 6.50 (d, 1H, $J$ = 9.5); 7.35–7.45 (m, $3H_{arom}$); 7.73 (d, 2H, $J$ = 7.4); 7.85 (s, $1H_{arom}$); 8.02 (d, 1H, $J$ = 9.5) | 305 ($M^+$, 100); 280 (45) |
| **2d** | 78 | 212–213 | $C_{19}H_{14}BrNO_3$ (384.2) | 1675 | 3.98, 4.04 (2s, 3H each, $OCH_3$); 6.41 (s, $1H_{arom}$); 6.50 (d, 1H, $J$ = 9.5); 7.55 (d, 2H, $J$ = 8.4); 7.58 (d, 2H, $J$ = 8.4); 7.84 (s, $1H_{arom}$); 8.04 (d, 1H, $J$ = 9.5) | 385/383 ($M^+$, 100); 371/369 (32); 289 (84) |
| **2e** | 92 | 183–184 | $C_{14}H_{13}NO_3$ (243.3) | 1671 | 2.44 (s, 3H, $CH_3$); 4.00, 4.02 (2s, 3H each, $OCH_3$); 6.32 (s, $1H_{arom}$); 6.45 (d, 1H, $J$ = 9.5); 7.48 (s, $1H_{arom}$); 7.94 (d, 1H, $J$ = 9.5) | 243 ($M^+$, 100); 228 (100); 200 (22); 185 (20) |
| **2f** | 95 | 189–190 | $C_{17}H_{17}NO_3$ (283.3) | 1669 | 1.80–1.91 (m, 4H, $CH_2$); 2.84–2.87 (m, 2H, $CH_2$); 3.23–3.27 (m, 2H, $CH_2$); 3.98, 3.99 (2s, 3H each, $OCH_3$); 6.33 (s, $1H_{arom}$); 6.40 (d, 1H, $J$ = 9.4); 7.91 (d, 1H, $J$ = 9.4) | 283 ($M^+$, 58); 268 (100) |

[a] Yield of isolated pure product.
[b] Uncorrected, measured with a Kofler melting point apparatus.
[c] Satisfactory microanalyses obtained: C ±0.30, H ±0.30, N ±0.30.
[d] Recorded on a Perkin-Elmer 580B spectrophotometer.
[e] Recorded at 500 MHz using a Bruker instrument.
[f] Recorded with an AE-1 mass spectrometer (MS12).

Attempts to prepare the compound **2** by a Perkin reaction,[12] refluxing 7-formylindole **1** with acetic anhydride in the presence of sodium acetate were not successful, and only traces of the pyrroloquinolones were detected.

**7,9-Dimethoxy-4-oxo-4*H*-pyrrolo[3,2,1-*ij*]quinolines (2); General Procedure:**

NaOEt (0.27 g, 4 mmol) is added to a stirred solution of 4,6-dimethoxy-7-formylindole[11] (0.205 g, 1 mmol) in dry EtOAc (15 mL). After refluxing for 6 h the solvent is evaporated. The residue is diluted with $H_2O$ (40 mL) and acidified with 2N HCl (2 mL). The suspension is extracted with $CH_2Cl_2$ (3 × 30 mL), dried ($Na_2SO_4$), evaporated, and recrystallized from $CH_2Cl_2$/MeOH (1:3) to yield compound **2** (Table).

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