Synthesis of 5-Methoxycarbonyl-11-methylfuro(2,3-c)acridan-6(11H)ones

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Furoacridanone Alkaloids, 1-Methyl-2-chloro-3(1-methoxycarbonyl-2(furo-2-yl)-1-ethenyl)quinolin-4(1H)ones, 5-Methoxycarbonyl-11-methylfuro(2,3-c)-acridan-6(11H)ones

A convenient photochemical route to 11-methylfuro(2,3-c)-acridan-6(11H)ones is reported.

The plant family Rutaceae is known [1, 2] to be a prolific source of furoquinoline and pyranoquinoline alkaloids. Along with them acridine alkaloids [3, 4] have also been isolated from several members of the same plant family. Recently furan-fused acridine systems such as 11-methylfuro(2,3-c)-acridan-6(11H)one (1) have also been reported [5-7] to occur in some rutaceous plants. Typical examples of its naturally occurring derivatives are the alkaloids furofoline-I (2) [6, 7] and furofoline-II (3) [7].

\[\begin{align*}
1: & \quad R^1 = R^2 = R^3 = H \\
2: & \quad R^1 = R^3 = H, R^2 = OH \\
3: & \quad R^1 = C(CH_3)_2-OH, R^2 = OH, R^3 = H \\
4a: & \quad R^1 = R^3 = H, R^2 = COOCH_3 \\
4b: & \quad R^1 = H, R^2 = COOCH_3, R^3 = Br
\end{align*}\]

In this communication we report a facile method for the construction of the titled system (4). It is based on a photochemical exploitation of the furylidene precursor such as 9a, which in turn was derived neatly as a result of a four-step sequence starting with a condensation reaction of furfural with 4-hydroxy-2-quinolinone-3-acetic acid (5a) [8] in a boiling mixture of acetic acid and acetic anhydride. The condensation product, realized in 86% yield as a yellow crystalline solid, was identified to be the angular furylidene lactone 6a on the basis of its IR spectrum which exhibited two bands in the carbonyl region one at 1775 cm\(^{-1}\) and the other at 1650 cm\(^{-1}\) ascribable respectively to a lactone carbonyl and a 2-quinolinone [9] moiety. A brief treatment of 6a with phosphoryl chloride gave the chloroquinoline 7a, the structure of which was confirmed by its spectral characteristics and analytical data. On boiling with methanol in the presence of concentrated sulphuric acid the lactone 7a cleaved to give the 4-hydroxyquinoline 8a which was N-methylated to 9a by treatment with methyl iodide in the presence of eight mole-equivalent of potassium carbonate in acetone.

Irradiation of a solution of 9a in benzene under non-oxidative conditions in a Rayonet Preparative Photoreactor gave, in 60% yield, a white crystal-
line solid. It was identified to be the anticipated photoproduct viz., 5-methoxycarbonyl-11-methyl-6-acridan(11H)one 4a resulting from dehydrochlorocyclization [10] of 9a. The correctness of the structure 4a assigned for the product was fully attested by analytical and spectral data obtained on it. The IR spectrum exhibited two carbonyl frequencies one at 1720 cm⁻¹ and the other at 1615 cm⁻¹ which were ascribed respectively to a methoxycarbonyl and a 4-quinolinone [9] groups.

Extension of the technique to 6-bromo-2-quinolinone-3-acetic acid (5b) also afforded the corresponding bromofuroacridanone 4b. The characteristic [11, 12] low-field absorption of the C₅-proton of quinolin-4(1H)one system is discernable in the ¹H NMR spectra of 4, 8 and 9.

The physical and spectral data obtained for all the compounds are summarized in Table I.

**Experimental**

3-Furylidene-2,4-dioxo-2,3,4,5-tetrahydrofuro(3,2-c)quinoline (6)

**General procedure**

A mixture of 4-hydroxy-2-quinolinone-3-acetic acid (4, 0.04 mol), acetic acid (20 ml), acetic anhydride (25 ml) and furfural (4 ml, 0.045 mol) was refluxed in an oil bath for 5 h. After cooling, the precipitated angular lactone 6 was isolated by suction, washed with chloroform, dried and recrystallized from 95% ethanol as yellow crystalline powder. The yield, m. p. etc., are given in Table I.

Table I. The physical and spectral data of the compounds 4, 6, 7, 8, and 9 prepared.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield (%)</th>
<th>M. p. (°C)a</th>
<th>Molecular formulab</th>
<th>IR (KBr) v (cm⁻¹)</th>
<th>¹H NMR (Solvent) δ (ppm)</th>
<th>Mass M+ (m/e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>86</td>
<td>&gt;300</td>
<td>C₁₄H₁₉NO₄</td>
<td>2800 (br), 1775, 1650</td>
<td>(DMSO-D₆): 6.88–8.28 (m, 8 H), 12.18 (br, s, 1H)</td>
<td>279</td>
</tr>
<tr>
<td>6b</td>
<td>85</td>
<td>&gt;300</td>
<td>C₁₄H₂BrNO₄</td>
<td>2800 (br), 1775, 1650</td>
<td>Insufficiently soluble</td>
<td>358</td>
</tr>
<tr>
<td>7a</td>
<td>88</td>
<td>213</td>
<td>C₁₄H₁₉CINO₄</td>
<td>1775, 1625</td>
<td>(CDCl₃): 6.75 (m, 1 H, J = 2), 7.65 (m, 1 H), 7.8 (m, 2 H), 8.1 (dd, 2 H), 8.4 (d, 1 H, J = 7), 8.5 (s, 1 H)</td>
<td>297</td>
</tr>
<tr>
<td>8b</td>
<td>92</td>
<td>244</td>
<td>C₁₄H₂BrCINO₄</td>
<td>2600–3000 (br)</td>
<td>(DMSO-D₆): 6.65 (s, 3 H), 6.85 (s, 1 H), 7.2–7.75 (m, 6 H), 8.02 (d, 1 H, J = 8)</td>
<td>407</td>
</tr>
<tr>
<td>9a</td>
<td>73</td>
<td>188–190</td>
<td>C₁₄H₂CINO₄</td>
<td>1720, 1610</td>
<td>(CDCl₃): 3.75 (s, 3 H), 4.02 (s, 3 H), 6.51 (m, 1 H), 6.87 (s, 1 H), 7.4–7.55 (m, 3 H), 7.57 (s, 1 H), 7.71 (m, 1 H), 8.46 (dd, 1 H, J = 8, 2)</td>
<td>343</td>
</tr>
<tr>
<td>9b</td>
<td>70</td>
<td>172 (dec)</td>
<td>C₁₄H₂BrCINO₄</td>
<td>1720, 1620</td>
<td>(CDCl₃): 3.75 (s, 3 H), 4.01 (s, 3 H), 6.51 (m, 1 H), 6.84 (s, 1 H), 7.4–7.48 (m, 3 H), 7.49 (s, 1 H), 8.54 (d, 1 H, J = 2)</td>
<td>421</td>
</tr>
<tr>
<td>4a</td>
<td>60</td>
<td>185 (dec)</td>
<td>C₁₄H₁₉NO₄</td>
<td>1720, 1615</td>
<td>(CDCl₃): 4.06 (s, 3 H), 4.21 (s, 3 H), 7.3 (m, 2 H), 7.38 (s, 1 H), 7.54 (d, 1 H, J = 8), 7.73 (d, 1 H, J = 8), 7.78 (d, 1 H, J = 2), 8.47 (d, 1 H, J = 7)</td>
<td>307</td>
</tr>
<tr>
<td>4b</td>
<td>55</td>
<td>&gt;300</td>
<td>C₁₄H₁₉BrNO₄</td>
<td>1720, 1620</td>
<td>Insufficiently soluble</td>
<td>385</td>
</tr>
</tbody>
</table>

a Uncorrected, measured using Mettler-FP5 apparatus and a Boietius Microheating Table; b satisfactory microanalyses obtained: C ±0.23, H ±0.11.
4-Chloro-3-furylidene-2-oxo-2,3-dihydrofuro-(3,2-c)quinoline (7)

**General procedure**

A mixture of the lactone 6 (0.01 mol) and freshly distilled phosphoryl chloride (30 ml) was refluxed in an oil bath until a homogenous solution was obtained and then further heated for another 20 minutes. The mixture was cooled and poured into crushed ice. The solid formed was collected by suction, washed with water, dried and recrystallized from benzene to give 7 as yellow crystalline solid. The results are summarized in Table I.

2-Chloro-3(1-methoxycarbonyl-2(furo-2-yl)-1-ethenyl)quinolin-4(1H)one (8)

**General procedure**

A mixture of 7 (0.01 mol), absolute methanol (100 ml) and concentrated sulphuric acid (0.5 ml) was refluxed on a steam bath for 3 h, then concentrated to one third of its total volume, cooled and poured into ice water. The precipitated ester was collected by suction, dried and recrystallized from benzene/methanol (3:1) mixture to give 8 as pale yellow crystalline powder. Yield, m.p. etc., are given in Table I.

1-Methyl-2-chloro-3(1-methoxycarbonyl-2(furo-2-yl)-1-ethenyl)quinolin-4(1H)one (9)

**General procedure**

The mixture of 8 (0.001 mol), anhydrous potassium carbonate (0.008 mol, 1.1 g) and methyl iodide (3 ml) was taken in dry acetone (50 ml) and refluxed for 8 h. Then the solution was filtered off from the potassium carbonate, concentrated to small bulk, poured into water and extracted with chloroform. The chloroform extract was then dried (Na$_2$SO$_4$) and concentrated to give a oily residue which on column-chromatography over neutral-alumina (~150 mesh, 1 x 20 cm) using petrol-ether (60-80 °C): benzene (2:1) mixture as eluent to afford 9 as white cubic crystals. The results are summarized in Table I.

5-Methoxycarbonyl-11-methylfuro(2,3-c)acridan-6(1H)one (4)

**General photocyclization procedure**

A solution of the substrate 9 (1 mmol) in dry benzene (250 ml) was placed in a quartz tube which was purged with oxygen-free dry nitrogen for 30 minutes. It is then irradiated at $\lambda = 253.7$ nm with UV lamps in a Rayonet Preparative Photoreactor (RPR model-208) for 12 h. In the case of 9a the product 4a was isolated by evaporation of the reaction mixture and column-chromatography of the resulting residue on an neutral alumina column (15 x 1 cm, ~150 mesh) using petrol-ether (60-80 °C): benzene (1:2) mixture eluent. In the case of 9b the product 4b was rated as crystalline mass during irradiation was collected by filtration and dried. The m.p. etc., of the photoproducts are furnished Table I.

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