Furo-quinolines Part VII[1]

Another Approach to the Synthesis of Furo(2,3-b)quinolines

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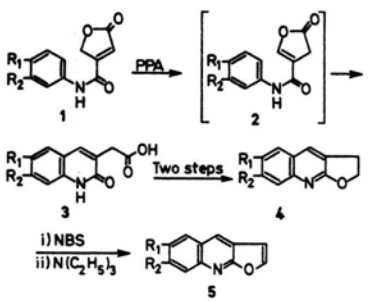
Aconanilides, 2-quinolone-3-aceticacids, dihydrofuro (2,3-b)quinolines, furo(2,3-b)quinolines

In our work reported previously[2,3] on the synthesis of 2,3-dihydrofuro(2,3-b)quinolines, we employed 2-quinolone-3-acetic acids as key intermediates. They were obtained from *o*-aminobenzaldehydes and ketones by acylation with succinic anhydride followed by ring closure with aq. alkali. The conversion, of the quinolone-acid to the corresponding dihydrofuroquinoline through reduction ($LiAlH_4$) of its ester followed by cyclization (PPA) of the resulting alcohol, is a neat and facile process. Since only a few *o*-aminobenzaldehydes were easily available, there was a corresponding limitation in our efforts to make, using this approach, various dihydrofuroquinolines of type **4**. Further the procedure involved in making the aminoaldehydes is rather cumbersome. Hence, it was felt that if a simple straight forward method, using aniline as the starting point, could be devised for the preparation of the key intermediates, *viz.*, the quinolone-acetic acids, this route to furo(2,3-b)quinolines could be made more expedient and widely applicable.



a $R_1=R_2=H$; b $R_1=R_2=OCH_3$

We wish to record another synthesis of the title compound **5a** and its 6:7 dimethoxy derivative **5b** based on the preparation of the required quinolone-acids (**3a** and **3b**) by a novel-one-step procedure and on the transformation of the dihydrofuroquinolines (**4a** and **4b**) derived from the respective acids.

Aconanilide (**1a**), prepared from aconyl chloride and aniline by a slight modification of the known procedure[4], furnished on heating with polyphosphoric acid an acid (45% yield) whose m.p. and IR spectrum (see experimental) corresponded to that of 2-quinolone-3-acetic acid[3] (**3a**). The acid and its ethyl ester were found to be identical with that of the authentic acid and its ester respectively. The aconanilide (**1b**), prepared from 3,4-dimethoxy aniline and aconylchloride likewise gave, on heating with PPA, the corresponding, 6,7-dimethoxy-2-quinolone-3-acetic acid (**3b**). Such a rearrangement involving aconanilides has not hither to been reported. The process presumably involves isomerisation of **1** to **2** and concomittant ring closure. This is an attractive method in that it is an one-step route from the anilide of readily accessible aconic acid[5].

The acids **3a** and **3b** were transformed into the dihydrofuroquinolines (**4a**)[3] and (**4b**)[2] respectively by the procedures previously reported. Treatment of **4a** with *N*-bromo-succinimide followed by heating with triethylamine in chloroform solution afforded the title compound (**5a**) in 33% yield. **4b** was likewise converted to 6,7-dimethoxyfuro(2,3-b)quinoline (**5b**) in 35% yield. **5a** as well as **5b** was found to be identical with the authentic sample[1] prepared from the corresponding 3-vinyl-2-quinolone.

Experimental

Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 337 spectrophotometer. NMR spectra were obtained on a Varian A-60 spectrometer in $CDCl_3$ solution using TMS as internal standard.

Aconanilide (**1a**)

3.2 g aconic acid[5] was refluxed with 7 ml purified thionyl chloride till it formed a solution (3 hours). The excess reagent was removed under reduced pressure and the residue was taken up in dry benzene and slowly added to an ice cold benzene solution containing 2.33 g aniline and 2.2 g pyridine. It was shaken well during the addition. It was set aside for a few minutes and poured into ice water. The precipitated solid was collected, dried and recrystallized from benzene containing little alcohol when **1a** was obtained as colourless crystals m.p. 181 °C. IR (KBr) 1674 cm^{-1} (NH · CO), a doublet[6] at 1739 and 1795 cm^{-1}.

2-quinolone-3-acetic acid (**3a**)

2 g **1a** was mixed with 7 ml polyphosphoric acid and heated in an oil bath at 120—125 °C for 3 hours. After cooling, it was poured into ice water. The

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precipitated solid was collected, washed successively with water and ice-cold ethanol. Recrystallization of the residue from acetic acid yielded **3a** as sandy powder yield 0.9 g (45%) m.p. 277—278 °C (dec). IR (KBr) 1700, 1645 and 1615 cm^{-1}.
$C_{11}H_9NO_3$ (203.2)
Calcd.: C 65.02 H 4.46,
Found: C 64.7 H 4.8.

Identical with the authentic acid[3] (m.p., mixed m.p., superimposable IR).

Ethylester of **3a**

m.p. 186—187 °C (ethanol) IR (KBr) 1730, 1670 and 1615 cm^{-1}.
$C_{13}H_{13}NO_3$ (231.3)
Calcd.: C 67.52 H 5.67,
Found: C 67.3 H 5.8.

Identical with the authentic ester (m.p., mixed m.p., superimposable IR).

2,3-Dihydrofuro(2,3-b)quinoline (**4a**)

Obtained from **3a** as described[3] before.

NMR: δ (ppm) 3.16 (*t*, 2 H, H_3) $J = 8$ cps; 4.55 (*t*, 2 H, H_2) $J = 8$ cps, 7.1 to 7.9 (m, 5 H, H_4 and the phenyl protons).

Furo(2,3-b)quinoline (**5a**)

To a solution of 200 mg **4a** in 20 ml carbontetrachloride, was added 200 mg *N*-bromosuccinimide followed by a crystal of benzoylperoxide. The solution was kept at reflux for half an hour and then cooled. The precipitated succinimide was removed and to the filtrate 20 ml chloroform and 10 ml triethylamine were added. The mixture was refluxed on a steambath for one hour. The amine hydrochloride was filtered off and the filtrate was evaporated to dryness under reduced pressure. The residue was chromatographed over alumina in petrol-benzene (1 : 1).

Recrystallization from petrol, gave **5a** as fine colourless needles (59 mg 33%) m.p. 78—79 °C.
$C_{11}H_7NO$ (169.2)
Calcd.: C 78.09 H 4.17,
Found: C 78.5 H 4.4.

Identical with the authentic sample[1] (m.p., mixed m.p., IR, UV, NMR, tlc).

Acon-3,4-dimethoxyanilide (**1b**)

Prepared from 3,4-dimethoxyaniline and aconic acid by a similar procedure adopted for **1a**.
m.p. 183—184 °C (ethanol); IR (KBr) 1667 cm^{-1} (NHCO) and a doublet[6] at 1786 and 1736 cm^{-1}.
$C_{13}H_{13}NO_5$ (263.3)
Calcd.: C 59.31 H 4.98,
Found: C 59.1 H 5.2.

6,7-Dimethoxy-2-quinolone-3-acetic acid (**3b**)

Prepared from **1b** as in the case of **3a**. The product was recrystallized from ethanol-acetic acid as colourless crystals; m.p. 262—264 °C (dec.); IR (KBr) 1675, 1645 and 1615 cm^{-1}.
$C_{13}H^{17}NO_5$ (263.3)
Calcd.: C 59.31 H 4.98,
Found: C 58.9 H 5.2.

Identical with the authentic sample (m.p., mixed m.p., IR).

Ethylester

Prepared as described before[2] m.p. 225—226 °C (ethanol); IR (KBr) 1725, 1675 and 1630 cm^{-1}.
$C_{15}H_{17}NO_5$ (291.3)
Calcd.: C 61.85 H 5.88,
Found: C 61.66 H 6.01.

2,3-dihydro-6,7-dimethoxy furo-(2,3-b)quinoline (**4b**)

Prepared from **3b** as described[2] before; NMR: δ (ppm) 3.25 (*t*, 2 H, H_3) $J = 8$ cps; 3.92 (S, 3 H, OCH_3), 3.97 (S, 3 H, OCH_3), 4.6 (*t*, 2 H, H_2) $J = 8$ cps; 6.88 (S, 1 H, H_8), 7.2 (S, 1 H, H_5) 7.58 (S, 1 H, H_4).

6,7-Dimethoxy furo(2,3-b)quinoline (**5b**)

231 mg **4b**, 200 mg NBS and a crystal of benzoylperoxide were heated in solution of carbontetrachloride-chloroform (1:1), at reflux for one hour. The reaction mixture was cooled and washed with water to remove the succinimide. After drying over anhydrous magnesium sulphate, the solution was evaporated, to dryness.

The residue was dissolved in 20 ml chloroform and mixed with 7 ml triethylamine and heated at reflux for 2 hours. The work up as in the previous case gave **5b** as brown solid. Chromatography over alumina in benzene afforded **5b** as colourless crystals. It was recrystallized from benzene-petrol (80 mg 35%) m.p. 172—173 °C.
$C_{13}H_{11}NO_3$ (229.2)
Calcd.: C 68.11 H 4.84,
Found: C 68.19 H 5.1.

Identical with the authentic sample[1] in all respects (m.p., mixed m.p., IR, UV, NMR and tlc).

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