

**SYNTHESIS OF  
3,4-DIHYDRO-4-METHYL-2-(QUINOLIN-3-YL)-2H-PYRANO[3,2-c]QUINOLINES**

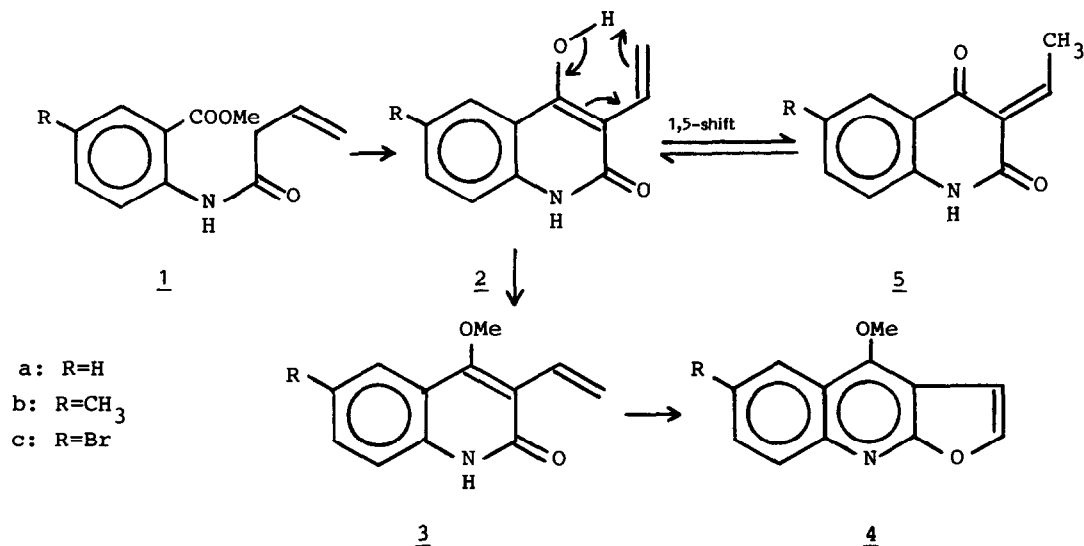
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Summary

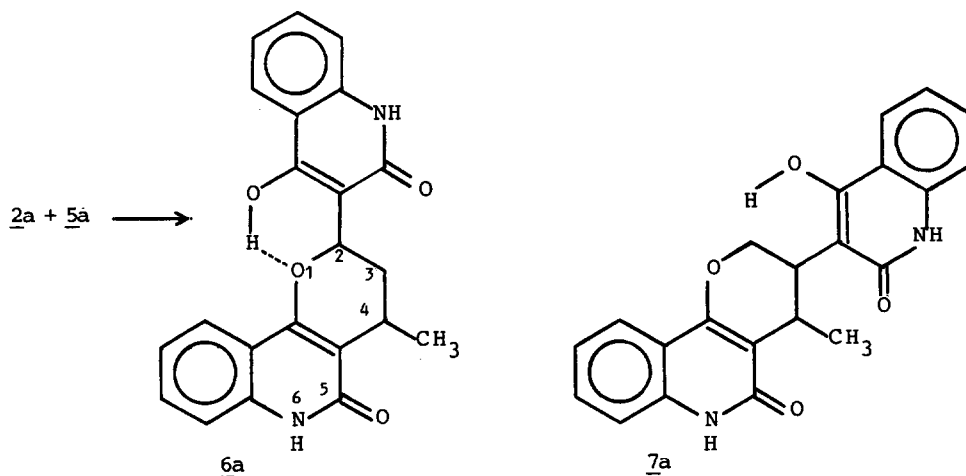
The attempted synthesis of 4-hydroxy-3-vinyl-2-quinolones(2), intended precursors for dictamnine and its derivatives(4), resulted in a cyclo-addition reaction leading to a dihydropyrano[3,2-c]quinoline system(6).

As a corollary to our realization, earlier reported<sup>1</sup>, of the synthesis of 3-vinyl-2-quinolones and from them the furo(2,3-b)quinoline system, which is well represented among the alkaloids of the Rutaceae<sup>2</sup>, we were interested in extending the synthetic programme to the naturally occurring derivatives, viz., the dictamnine group of alkaloids.

We prepared methyl N-(3-butenoyl)anthranilate(1a) and subjected it to a Dieckmann-cyclisation (using NaH in dry benzene or NaOMe in absolute methanol) as a plausible means to derive the hydroxyquinolone 2a, preparatory to the realization of the requisite precursor, viz., 3a for obtaining dictamnine (4a). A brown solid product was obtained on workup. Recrystallisation from glacial acetic acid furnished it as a pale brown powder (m.p. > 300° ; yield 70-80%). It readily went into solution in aqueous alkali and it was regenerated from the solution by bubbling through it carbon-dioxide. This, coupled with its reaction with neutral ferric chloride (in ethanol) giving reddish brown coloration, indicated it to be a phenol.

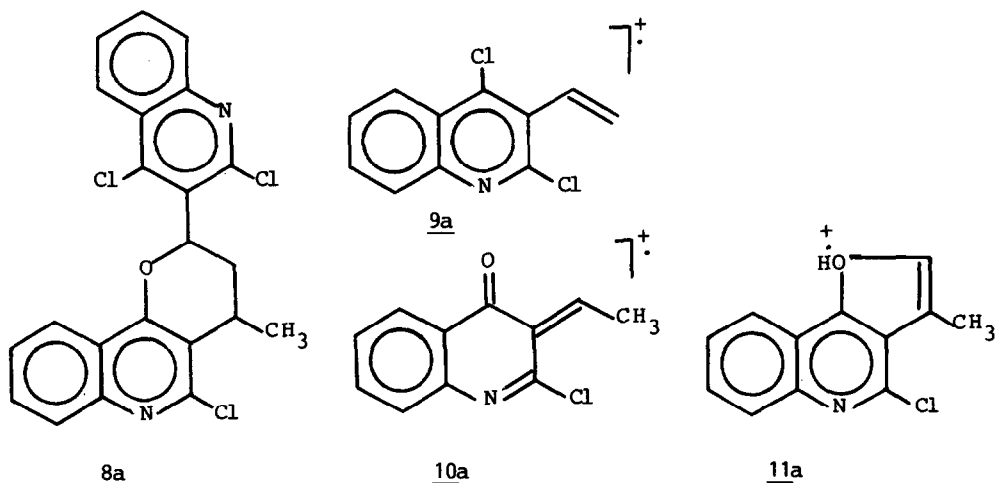


The analytical values are compatible with the molecular formula  $C_{11}H_9NO_2$  (as that of 2a). The i.r. spectrum showed an 'NHCO' band at  $1650\text{ cm}^{-1}$  and a sharp 'OH' band at  $3360\text{ cm}^{-1}$ . But the spectrum lacked the absorption expected<sup>3</sup> of a vinylic group in the region  $1000\text{--}900\text{ cm}^{-1}$ . The absence of the vinylic group in the product was further attested by its resistance to catalytic hydrogenation<sup>4</sup> ( $H_2$ , Pd/C 5or10% in ethanol) as well as reduction with NaHTe<sup>5</sup>. The  $^1H$ -n.m.r. spectrum of the compound taken in trifluoroacetic acid (insoluble in other spectral solvents) also did not register



the presence of a vinyl group<sup>6</sup>, but showed instead, a three-proton doublet at  $\delta = 1.60$ , an one-proton doublet of a doublet at  $\delta = 6.03$ , a three-proton multiplet at  $\delta = 1.90\text{--}3.50$  and an eight-proton aromatic envelope at  $\delta = 7.20\text{--}8.20$ . On the basis of this data, we inferred that a dimeric product of the type 6a or 7a could have emanated from the reaction. The reaction course apparently involved a cycloaddition of the vinyl in 2a with the heterodiene moiety present in the tautomer, viz., the quinone-methide(5a). Since in the i.r. spectrum the 'OH' appeared as hydrogen-bonded, the structure 6a [3,4-dihydro-2-(4-hydroxyquinolin-2(1H)-one-3-yl)-4-methyl-2H-pyrano[3,2-c]quinolin-5(6H)-one] is considered more probable than the regioisomeric structure 7a (which could be formed in an alternative mode of cycloaddition). Moreover, a low field one-proton doublet of a doublet at  $\delta = 6.03$  assignable<sup>7</sup> to  $C_2\text{-H}$  is in accord with the presence of adjacent Ar and ArO groups as in 6a. This constitutes an interesting example of a quinone-methide<sup>8</sup>, which is part of a heterocyclic system, undergoing an 1,4-cycloaddition with its vinylic tautomer serving as a suitable addendum, to give rise to a dihydropyran-condensed quinoline.

A convincing proof for the dimeric structure 6a was gained on the analysis of the white crystalline solid 8a (yield 55%; m.p. 216-217° benzene-petrol) obtained when it was treated with phosphoryl chloride. Its i.r. spectrum documented, as expected, the loss of the 'OH' as well as the 'NHCO' groups. The  $^1\text{H-n.m.r.}$  spectrum showed a three-proton doublet at  $\delta = 1.63$ , an one-proton doublet of a doublet at  $\delta = 6.38$ , a three-proton multiplet in the region  $\delta = 2.00-3.60$  and an eight-proton aromatic envelope at  $\delta = 7.25-8.37$ . The gross structure of the compound, 3,4-dihydro-5-chloro-4-methyl-2-(2,4-dichloroquinolin-3-yl)-2H-pyrano[3,2-c]quinoline (8a) was



indicated by the mass spectrum which showed molecular ion peak at  $m/e$  428 (88%). This as well as the values of the elemental analysis are in accord with the molecular formula  $\text{C}_{22}\text{H}_{15}\text{N}_2\text{OCl}_3$ . The base peak appeared at  $m/e$  218 ( $\text{C}_{12}\text{H}_9\text{NOCl}$ ) (11a). The fragment ions that appear at  $m/e$  223(71%) (9a) and at  $m/e$  205(67%) (10a) can be accounted on the basis of a retro Diels-Alder cleavage of the molecular ion.

A similar series of compounds were realized with 1b and 1c.

6b: Yield 70%; m.p.  $> 300^\circ$ ; M.F.  $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_4$ ; I.R.(KBr)  $\nu = 1660(\text{NHCO})$ ,  $3390(\text{OH}) \text{ cm}^{-1}$ .

8b: Yield 50%; m.p. 218-219° (benzene-petrol); M.F.  $\text{C}_{24}\text{H}_{19}\text{N}_2\text{OCl}_3$ ; M.S.  $m/e$  456(42%), 237(63%), 232(86%), 219(100%).  $^1\text{H-N.M.R.}$  ( $\text{CDCl}_3$ )  $\delta = 1.57(\text{d}, 3\text{H}, -\text{CH}-\text{CH}_3)$ ,  $2.40(\text{s}, 3\text{H}, \text{ArCH}_3)$ ,  $2.58(\text{s}, 3\text{H}, \text{ArCH}_3)$ ,  $6.35(\text{dd}, 1\text{H}, \text{Ar}-\text{O}-\text{CH}-\text{Ar})$ ,  $7.30-8.02(\text{m}, 6\text{H}, \text{ArH})$ ,  $1.85-3.45(\text{m}, 3\text{H}, -\text{CH}_2-\text{CH}-)$ .

6c: Yield 65%; m.p.  $> 330^\circ$ ; M.F.  $\text{C}_{22}\text{H}_{16}\text{N}_2\text{O}_4\text{Br}_2$ ; I.R.(KBr)  $\nu = 1650(\text{NHCO})$ ,  $3380(\text{OH}) \text{ cm}^{-1}$ .

8c: Yield 46%; m.p. 280° (benzene); M.F.  $C_{22}H_{13}N_2OBr_2Cl_3$ ;  
 M.S. m/e 586(27%), 509(100%), 301(19%), 296(44%), 283(50%).  
 $^1H$ -N.M.R. (DMSO- $d_6$ )  $\delta$  = 1.58(d, 3H,  $-CH-CH_3$ ), 1.82-3.35(m, 3H,  $-CH_2-CH-$ ),  
 6.25(dd, 1H, Ar-O- $\underset{|}{\underset{|}{CH}}$ -Ar), 7.25-8.0(m, 6H, ArH).

All the compounds gave satisfactory elemental analysis.

#### ACKNOWLEDGEMENT

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