

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

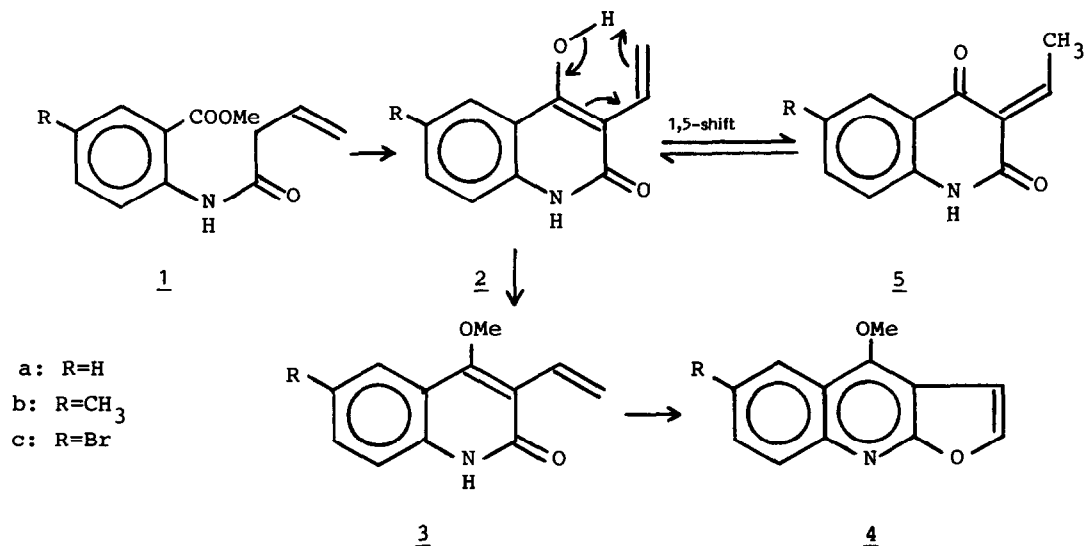
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Summary

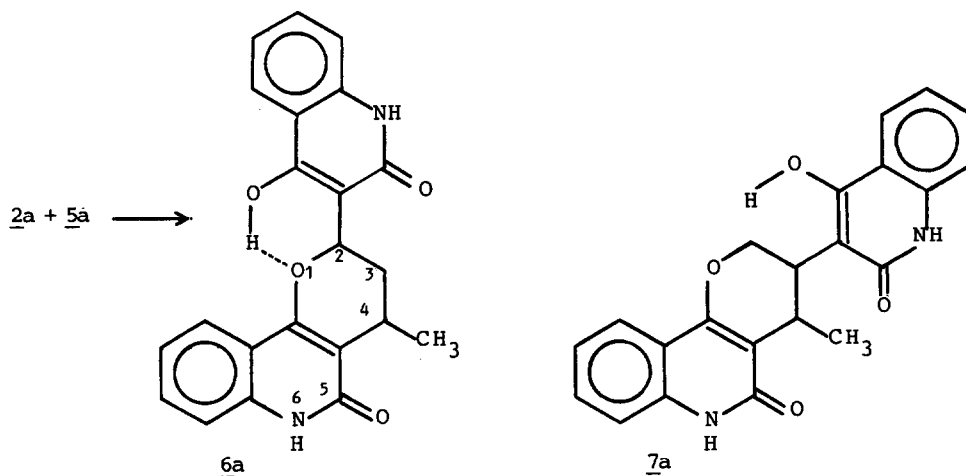
The attempted synthesis of 4-hydroxy-3-vinyl-2-quinolones(2), intended precursors for dictamnine and its derivatives(4), resulted in a cyclo-addition reaction leading to a dihydropyrano[3,2-c]quinoline system(6).

As a corollary to our realization, earlier reported¹, 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 Rutaceae², 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.

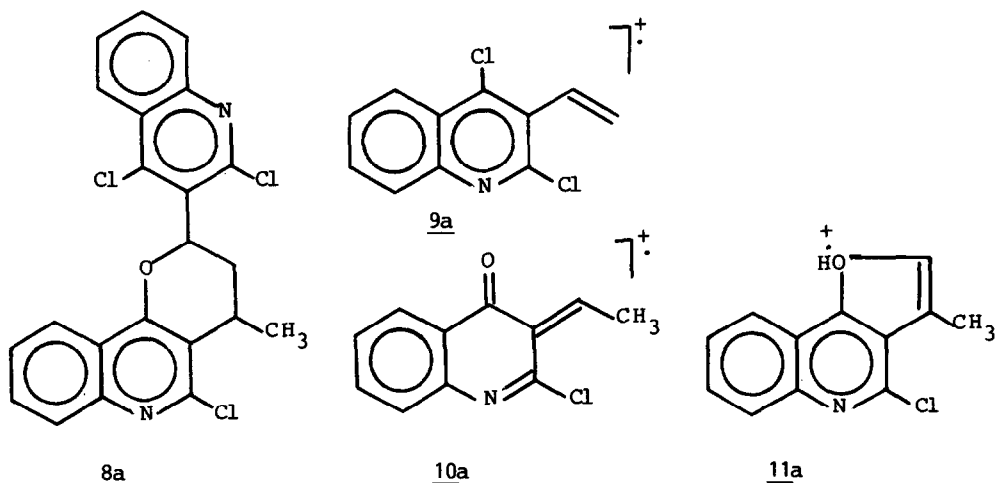


The analytical values are compatible with the molecular formula $C_{11}H_9NO_2$ (as that of 2a). The i.r. spectrum showed an 'NHC=O' band at 1650 cm^{-1} and a sharp 'OH' band at 3360 cm^{-1} . But the spectrum lacked the absorption expected³ of a vinylic group in the region $1000\text{--}900\text{ cm}^{-1}$. The absence of the vinylic group in the product was further attested by its resistance to catalytic hydrogenation⁴ (H_2 , Pd/C 5 or 10% in ethanol) as well as reduction with $NaHTe$ ⁵. 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 group⁶, 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 $\delta = 6.03$ assignable⁷ 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-methide⁸, 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 ¹H-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 $C_{22}H_{15}N_2OCl_3$. The base peak appeared at m/e 218 ($C_{12}H_9NOCl$) (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°; M.F. $C_{24}H_{22}N_2O_4$; I.R.(KBr) $\nu = 1660(NHCO)$, $3390(OH)$ cm^{-1} .

8b: Yield 50%; m.p. 218-219° (benzene-petrol); M.F. $C_{24}H_{19}N_2OCl_3$; M.S. m/e 456(42%), 237(63%), 232(86%), 219(100%). ¹H-N.M.R. ($CDCl_3$) $\delta = 1.57(d, 3H, -CH-CH_3)$, $2.40(s, 3H, ArCH_3)$, $2.58(s, 3H, ArCH_3)$, $6.35(dd, 1H, Ar-O-CH-Ar)$, $7.30-8.02(m, 6H, ArH)$, $1.85-3.45(m, 3H, -CH_2-CH-)$.

6c: Yield 65%; m.p. > 330°; M.F. $C_{22}H_{16}N_2O_4Br_2$; I.R.(KBr) $\nu = 1650(NHCO)$, $3380(OH)$ 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) δ = 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.

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