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A REVISED STRUCTURE FOR PONTEVEDRINE

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In the study of the alkaloids of Glaucium flavum Cr. var. vestitum two new oxoaporphines were isolated and assigned the novel 5,7-dioxoaporphine structure (II) to pontevedrine on the bases of spectroscopic data and chemical transformations (2). The 4,5-dioxoaporphine structure (I) was ruled out on the evidence of the reaction of O-Me-atheroline (VII) (a 7-oxoaporphine) with methyl iodide which afforded traces of pontevedrine. The isolation of cataline (III) (a C-4 hydroxylated aporphine) from the same source (3, 4) and its easy conversion into pontevedrine suggested that its structure ought to be reconsidered and we now conclude that the formulation of pontevedrine should be revised to that of (I).

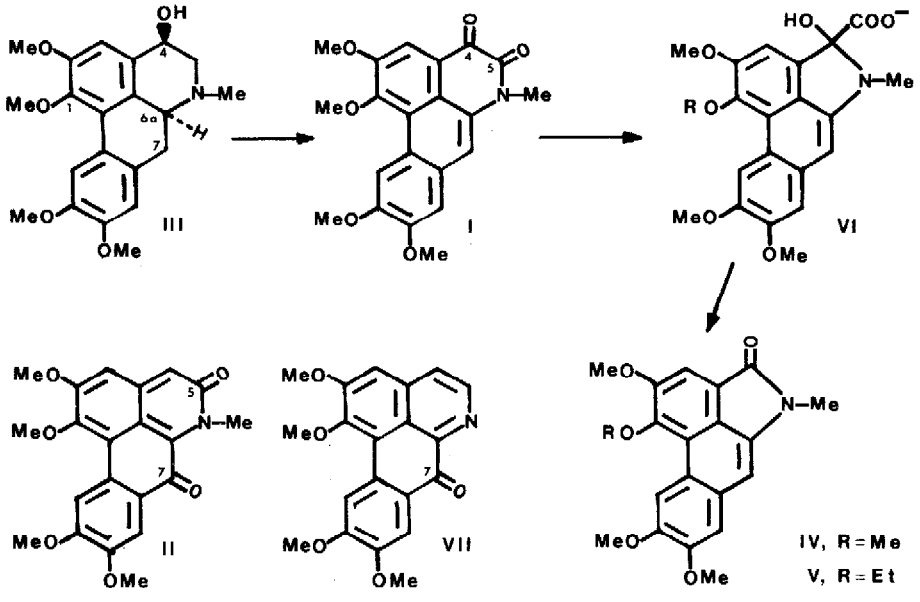
Thus re-examination of the mentioned reaction of highly purified O-Me-atheroline (VII) obtained from several sources (5, 6), gave no traces of pontevedrine. On the other hand, it is known that oxidation of aporphines with I_2/dioxane or DDQ (7) gives 6a-7 dehydroaporphines while 7-oxoaporphines are obtained under stronger oxidation conditions (8). Treatment of III with iodine or DDQ afforded pontevedrine (75-90%) while oxidation with lead tetraacetate or photo-oxidation gave VII.

From these results it can be assumed a 6a--7 double bond for pontevedrine and therefore the two carbonyl groups, whose presence was confirmed by C-13 NMR spectroscopy (9), should be located at C-4 and C-5. This assumption was proved by the fact that pontevedrine gives a benzilic acid rearrangement as has been observed in analogous systems (10), confirming the presence of the -CO-CO-NMe grouping.

Thus, treatment of pontevedrine with sodium hydroxide in methanol gave a yellow compound (IV) mp. 216-17°, 71%). Loss of a carbonyl group was obtained by an elementary analysis ($C_{20}H_{19}O_5N$) and mass spectrum (M^+ at m/e 353), being the pmr of (IV) similar to that of pontevedrine. It shows four aromatic hydrogens (singlets at δ 8.5, 7.5, 7.0 and 6.68 ppm), four aromatic -OMe groups (3.9 ppm) and one N-Me group (at 3.3 ppm). IV can be regarded as arising from the decarbonilation of the benzilic acid rearranged intermediate (VI). Any attempt to isolate VI was unsuccesful.

Surprisingly when the reaction was carried out with ethanol as solvent, a yellow product, V, (mp. 210-14°C, 57%) different from IV was isolated. The presence of an -OEt replacing an -OMe group was evident from the elementary analysis ($C_{21}H_{21}O_5N$), mass spectrum (M^+ at m/e 367) and pmr, which shows the $-CH_2-$(q, J = 7Hz) at 4.25 ppm., the $-CH_3$ (t, J = 7Hz) at 1.57 ppm. and only three -OMe at 3.9 ppm. Tentatively we assigned the C-1 position for the -OEt group in V, since its lability is known in 1,2-dimethoxyaporphines and oxoaporphines (11).

Pontevedrine (I) must be considered then a 4,5-dioxoaporphine, analogous to those recently described (12) IV and V might be classified as aristololactams-N-Methylated (13). Since aporphine alkaloids have been postulated



as precursors of aristololactams (14) in plants, the biosynthetic pathway can be enlarged with the introduction of the C–4 hydroxylated and the 4,5–dioxoaporphines as possible intermediates.

Work on the total synthesis of 4,5–dioxoaporphines and on this novel synthetic approach to aristololactams, are in progress.

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