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SYNTHESIS OF TETRA-O-METHYL DISTEMONANTHIN

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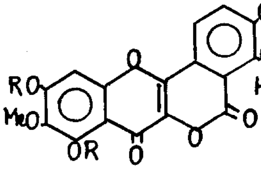
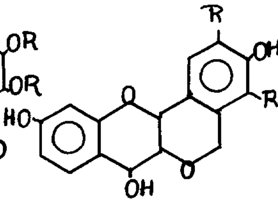
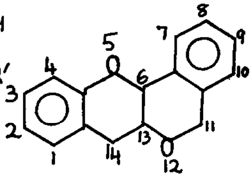
Distemonanthin is a yellow component of the wood of Distemonanthus benthamianus and has been given the structure of chromono (3',2'-3,4) isocoumarin (I)[1]. This ring system is rather rare in natural products; the closely related ones are peltogynol (II)[2,3] and mopanol (III)[4]. It is now suggested that the basic skeleton of these compounds may be called peltogynan with the numbering as shown in formula (IV), because peltogynol was the earliest[5] known member of the series. This is analogous to the skeleton of cyanomacluran recently discussed[6]. Each of them has a six-membered oxygen ring fused on either side to the B and C rings of the flavan molecule; in cyanomacluran the new linking is in the 4 position whereas in peltogynan it is in the 3 position. Distemonanthin would then be 1,3,9,10-tetrahydroxy-2-methoxy-6,13-dehydropeltogynan-11,14-dione.



I, R=H
V, R= Me



II, R= OH ; R'= H
III, R= H ; R'= OH



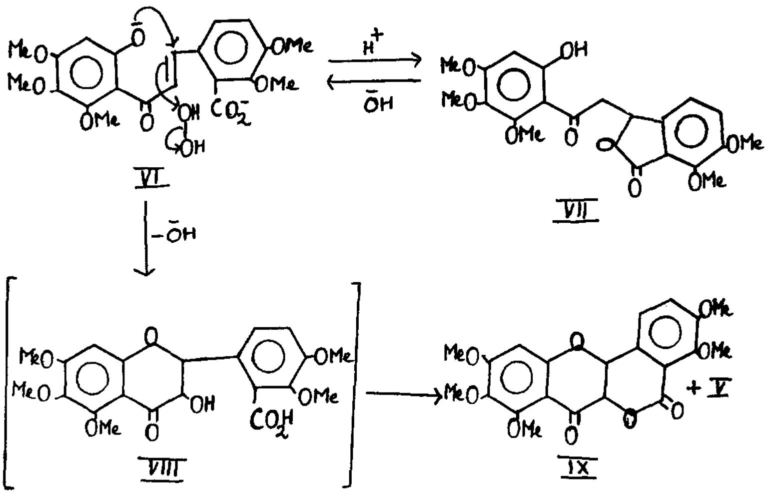
IV

Though several dehydropeltogynandiones have been made earlier, neither distemonanthin nor any of its derivatives have been synthesised so far. The synthesis of its complete methyl ether (V) has now been accomplished. Earlier King et al[1]. adopted the Baker-Venkataraman method using ω-methoxyresacetophenone and ω-methoxyphloroacetophenone as the ketonic components and the half ester-acid chloride of phthalic acid as the acylating agent. The resulting 3-methoxyflavone-2'-carboxylic acids were subjected to demethylative cyclisation. This method has, however, not been further used.

Later Venturella and Bellino[7] adopted chalkone condensation and subsequent oxidation with alkaline hydrogen peroxide. They employed 2-hydroxyacetophenone and its mono- and dimethoxy derivatives as ketonic components and phthalaldehydic acid as the aldehydic component. More recently, peonol has been condensed with *m*-opianic acid and the resulting chalkone-2-carboxylic acid oxidised to give 3,8,9-trimethoxy-6, 13-dehydropeltogynan-11,14-dione[8,9].

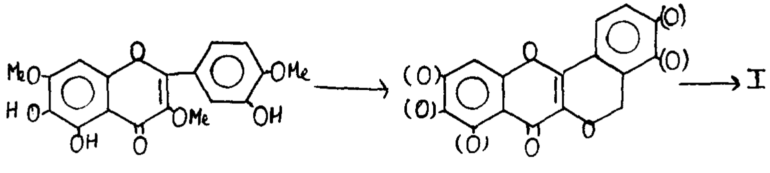
As the chalkone method is more suitable for the synthesis of tetra-*O*-methyl distemonanthin (V), we have used it and condensed 2-hydroxy,4,5,6-trimethoxyacetophenone[10] with opianic acid in the presence of aqueous ethanolic alkali when the phthalide (VII m.p.178-79°) was obtained in very good yields, λ_{max} ($CHCl_3$): 286 mμ(log ϵ 3.11); λ_{max} (0.1 N.NaOH): 233-244 (infl.), 330, 398-406 mμ(infl.) (logϵ 4.14, 4.25, 3.57); ν_{max} (nujol): 1773 (phthalide CO), 1628 cm^{-1} (chelated carbonyl). The corresponding chalkone (VI) is found only in very small amounts and has obviously been largely converted into the phthalide. However, the phthalide behaves as a chalkone when subjected to oxidation with alkaline hydrogen peroxide; subsequent acidification yielded two products. One was identified as tetra-*O*-methyl distemonanthin (V) (m.p.271-72°), λ_{max} ($CHCl_3$):

260 (infl.), 294 (infl.), 338, 349 mμ(log ε 4.03, 3.85, 4.19, 4.17), λ_{max} (0.1 N 90% ethanolic NaOH): 258-266 (infl.), 310, 386-394 mμ(log ε 4.11, 3.67, 4.02); ν_{max} (mujol): 1740 (lactone CO), 1655 cm^{-1} (chromone CO). All these properties are in agreement with those described in the literature.[1] The other product is its dihydroderivative (IX), as shown by the characteristic UV spectrum λ_{max} (CHCl$_3$): 290, 325 mμ(log ε 3.74, 4.15); λ_{max} (0.1 N. 90% ethanolic NaOH): 280, 340 mμ (log ε 4.05, 3.68) and the I.R. spectrum ν_{max} (mujol): 1763 (lactone CO), 1735 cm^{-1} (flavanone CO).



No aurone seemed to be formed in this reaction. This is unexpected in view of the presence of the 6'-methoxyl in the chalkone[11]. However, such behaviour during A.F.O. reaction finds analogy in that of 6'-substituted chalkones having free phenolic hydroxyls in the ring B at either 2 or 4 positions; in these cases also flavonols are formed and no aurones are obtained[12]. The explanation of this action in the present case could be similar to that given by Dean and Podimuang[13] for the above mentioned cases. The monohydroxy-carboxychalkone (VI) exists mainly as a doubly charged anion in alkali and consequently owing to repulsion of charges, hydrogen peroxide cannot approach it as an anion but as a neutral molecule. The dianion then eliminates one of its charges as a part of the process as shown in formula (VI). The dihydroflavonol carboxylic acid (VIII) thus formed undergoes either just lactonisation to give (IX) or both dehydrogenation and lactonisation to afford (V). The above synthesis thus confirms the ring system and oxygenation pattern of distemonanthin. The synthesis of distemonanthin itself is in progress.

During the progress of this work, the recent publication of Renault and Mentzer[14] reached us. They have also condensed opianic acid but with the simple ketones o-hydroxy acetophenone and peonol. They hydrolysed the phthalides into chalkone-2-carboxylic acids as a preliminary step and then carried out oxidation with alkaline hydrogen peroxide; we do not, however, find this necessary.

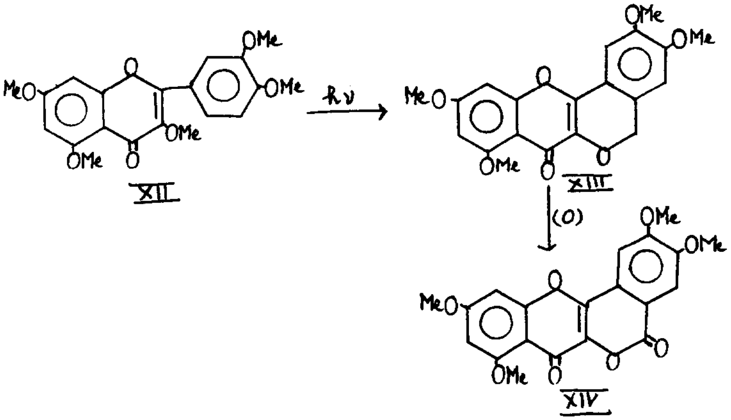


X

XI

The occurrence of distemonanthin along with related flavonoids and particularly oxyayanin-B may have significance in biogenesis. The simpler oxyayanin-B (X) could be visualised as undergoing oxidative cyclisation to yield distemonanthin (I) as indicated in the above formulae. An analogous example which has recently[15] been discussed is the evolution of rotenoids from the related isoflavanones. For example, toxicarol isoflavone which is found along with the rotenoid toxicarol is considered to give rise to the latter by the 2'-methoxy group taking part in oxidation with a reactive methylene group. In the present case, it is the aromatic position which has similar reactivity being activated by the nuclear methoxy group.

In further support of the above scheme, the experiments of Waiss and Corse[16] may be significant. They converted penta-O-methyl quercetin (XII) by photochemical method into 6,13-dehydropeltogynan-11-one (XIII) and subsequently into dione (XIV) by mild oxidation.



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