Immediate Biogenetic Precursors of Mopanols and Peltogynols

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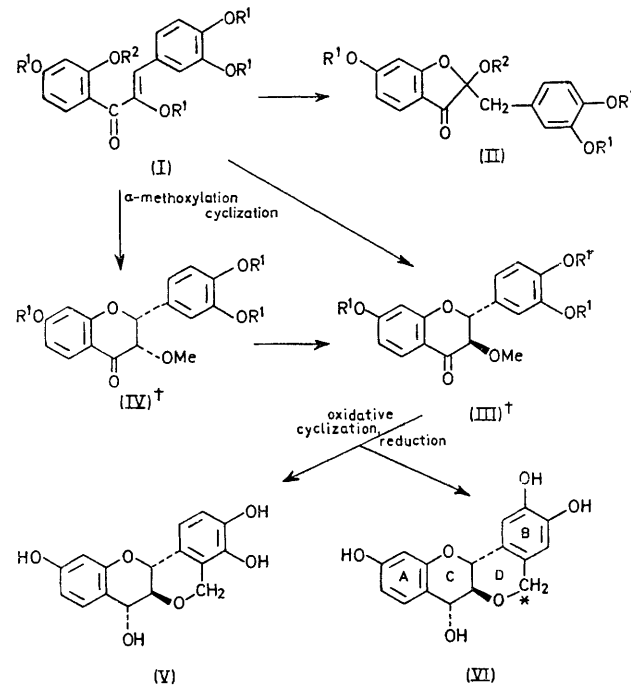
Summary α,2′,3,4,4′-Pentahydroxychalcone and 3-*O*-methyl-2,3-*trans*-fustin, associated with 3-*O*-methyl-2,3-*cis*-fustin and a 2-benzylcoumaranone analogue, are the presumed precursors of (+)-mopanol and (+)-peltogynol, and their 4-epimers, in the heartwood of *Trachylobium verrucosum* (Gaertn.) Oliv.

SUGGESTIONS regarding the origin of the "extra" skeletal carbon atom in the D-ring of peltogynol[1-3] (VI, marked by an asterisk) may be divided into two categories, (i) those which favoured introduction at the 6′-position of a CH_2OH grouping, derived variously through addition of formaldehyde or its equivalent,[2] or biochemical reduction of a carboxy-group derived, for example, from shikimic acid[4] by the method which Wenkert and Bringi[5] invoked in their theory of indole alkaloid biosynthesis; and (ii) the inference by Waiss and Corse[6] that 3-methoxy-function is responsible for D-ring formation, based on their observation of the photo-oxidative cyclization of pentamethoxyquercetin.

New credence is given to some aspects of the latter theory by the isolation from the heartwood of *Trachylobium verrucosum*, the gum copal tree from the coastal regions of Eastern Malagasy and East Africa, of both (+)-peltogynol (VI)[3,7] and (+)-mopanol (V)[3,7] and their 4-epimers, isopeltogynol[2,3,7] and isomopanol[3,7] associated with α,2′,3,4,4′-pentahydroxychalcone (I; $R^1 = R^2 = H$), 2-methoxy-3′,4′,6-trihydroxy- (II; $R^1 = H$, $R^2 = Me$) or 2,3′,4′,6-tetrahydroxy-2-benzylcoumaranone (II; $R^1 = R^2 = H$),3-*O*-methyl-2,3-*trans*-fustin, m.p. 143° (III; $R^1 = H$) ($J_{2,3}$ 10·4 Hz), and 3-*O*-methyl-2,3-*cis*-fustin (IV; $R^1 = H$) ($J_{2,3}$ 2·0 Hz). These compounds were characterized by their partial (I; $R^1 = Me$, $R^2 = H$) or full methyl ethers (II—IV, $R^1 = R^2 = Me$) after methylation with diazomethane. Proof of the presence or otherwise of methoxy-groups in the appropriate positions was obtained through the acetates of (I; $R^1 = R^2 = Ac$) and (III and IV; $R^1 = Ac$) and from the full methyl ethers of the fustins (III, IV; $R^1 = Me$), since prolonged treatment of fustin with diazomethane does not give methylation of the 3-hydroxy-group.[8] The acetate of the 2-benzylcoumaranone analogue (II), by far the least prominent of these, could not be isolated.

Most of the new compounds are amorphous, but proof of structure was provided by synthesis followed by n.m.r. and mass spectral comparisons. 2′-Hydroxy-α,3,4,4′-tetramethoxychalcone (I; $R^1 = Me$, $R^2 = H$), obtained by treatment of 2-hydroxy-ω,4-dimethoxyacetophenone with 3,4-dimethoxybenzaldehyde, was cyclized under different conditions[9,10] to give both 2,3′,4′,6-tetramethoxy-2-benzylcoumaranone (II; $R^1 = R^2 = Me$) and 3,3′,4′,7-*O*-tetramethyl-2,3-*trans*-fustin (III; $R^1 = Me$).‡ The latter was also prepared by full methylation of natural (±)-fustin from *Rhus glabra*[8] with Me_2SO_4–K_2CO_3 in acetone. Ring opening of *O*-tetramethylfustin (III; $R^1 = Me$) with alkali again gave the corresponding 2′-hydroxy-α-methoxychalcone (I; $R^1 = Me$, $R^2 = H$).



SCHEME

The natural compounds could have common biogenetic origins (see Scheme) in the α-hydroxychalcone (I; $R^1 = R^2 = H$), the (+)-mopanols (V, and 4-epimer), and (+)-peltogynols (VI, and 4-epimer) representing alternative structures derived presumably from oxidative cyclization of optically active 3-methoxy-2,3-*trans*-fustin (III), followed by reduction. This cyclization must be enzymic since the compounds originate at the sapwood–heartwood interface where no photochemical effect[6] is possible.

On the above assumption methylation of the α-hydroxy-group of the chalcone (I; $R^1 = R^2 = H$) apparently occurs before its conversion into 3-*O*-methyl-2,3-*trans*- and 3-*O*-methyl-2,3-*cis*-fustins (III and IV; $R^1 = H$). The suggested conversion of 2,3-*cis*- into 2,3-*trans*-fustins, due to greater thermodynamic stability of the latter,[10] requires inversion at C-3, probably *via* protonation of the 4-carbonyl group.[11] The relative ease of racemization of dihydroflavonols, requiring simultaneous inversions at both C-2 and C-3, rationalizes the optical inactivity of both fustins

† (III) and (IV) are racemates; only one enantiomer of each is illustrated.

‡ *Added in Proof:* Cyclization of 2′-hydroxy-α,3,4,4′-tetramethoxychalcone (I; $R^1 = Me$, $R^2 = H$) with sodium acetate in ethanol gives both 3,3′,4′,7-*O*-tetramethyl-2,3-*cis*-fustin (IV; $R^1 = Me$) and 3,3′,4′,7-*O*-tetramethyl-2,3-*trans*-fustin (III; $R' = Me$) in the proportion of 1 : 2.

(III and IV; R^1 = H), presumably as a result of ageing in the heartwood. This contrasts with the optical purity of the associated mopanols and peltogynols where stable chiral centres exist at corresponding positions.

Our work represents the first isolation of a natural α-hydroxychalcone, 3-*O*-methyldihydroflavonols, and a 2,3-*cis*-dihydroflavonol, the latter representing a class of compound which was synthesized only recently.[10]

As assistantship (J.P.v.d.M.) and bursary (E.V.B.) by the South African Council for Scientific and Industrial Research, Pretoria, and also the tenure of a senior fellowship by the South African Industrial Cellulose Corporation (E.V.B.), are acknowledged.

(*Received*, 14*th February* 1972; *Com.* 233.)

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