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TWO NEW FLAVONES FROM ARTOCARPUS HETEROPHYLLUS

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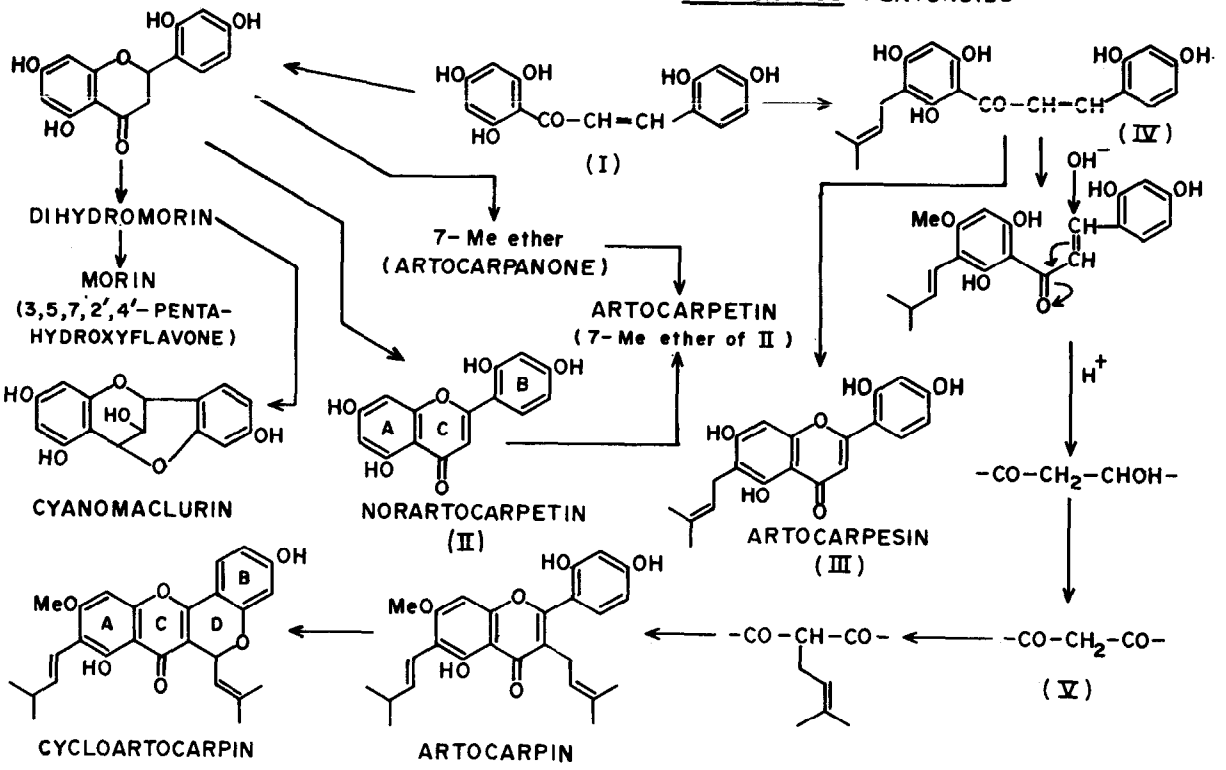
From a relatively young heartwood of A. heterophyllus Lamarck (now regarded as the correct name for the Jack tree, formerly called A. integrifolia)[1] we have isolated two new flavones, norartocarpetin (II) and artocarpesin (III); the wood also contained artocarpanone, artocarpin, cycloartocarpin, morin and cyanomaclurin, but no artocarpetin and dihydromorin.[2] Like the other seven flavonoids of A. heterophyllus, (II) and (III) have the unique β-resorcylic acid orientation of hydroxyl groups in the B-ring, not present in any other flavonoids, except the isoflavones ferreirin and homoferreirin. In connection with the biosynthesis of 7-oxygenated coumarins Austin and Meyers[3] have recently suggested that "the O-glucosylation of the product of enzymic orthohydroxylation of the trans-cinnamic system plays a key part in the ensuing stereomutation to the cis-o-glucoside"; A. heterophyllus apparently possesses the mechanism for directing the glucoside of 2,4-dihydroxy-trans-cinnamic acid to an alternative pathway in which it condenses with acetate-malonate units to form the chalcone (I). The nine flavonoids fit into a biosynthetic scheme (Chart 1) in which the hydroxylation pattern of both the A and B rings is fixed at the chalcone stage (I).[4] Attack of the phloro-

CHART 1. BIOSYNTHESIS OF ARTOCARPUS FLAVONOIDS



glucinol nucleus by one unit of 3,3-dimethylallyl pyrophosphate[5] leads to (IV) and artocarpesin (III). The dibenzoylmethane (V) may be formed as indicated, and attack by a second unit of dimethylallyl pyrophosphate, followed by cyclization and shift of an olefinic bond to conjugate with the benzene ring, will lead to artocarpin. Further cyclization of artocarpin to cycloartocarpin involves the oxidation of the doubly allylic CH_2 to CHOH.

The new pigments were first detected by thin layer chromatography on silica gel using acetone-benzene (1:3) as solvent. Artocarpesin separated from the ethyl acetate extract and successive crystallization from acetone and methanol gave yellow needles, m.p. 250°. The residue from the ethyl acetate extract was mixed with the exhausted wood and successively extracted with hexane, benzene and ethyl acetate. The last led to a mixture of morin, cyanomaclurin and norartocarpetin (II), from which the first two were separated by treatment with acetone; (II) crystallized from acetone in pale yellow needles (decomp. at about 330°).

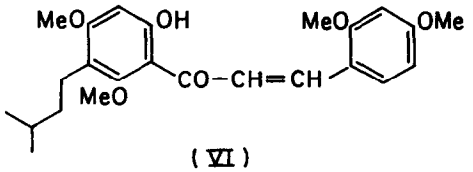
Direct comparison of norartocarpetin tetramethyl ether with synthetic 5,7,2',4'-tetramethoxyflavone[6] readily proved that norartocarpetin has the structure (II). The NMR spectrum of the ether in $CDCl_3$ showed four methoxyl groups at 6.05, 6.09, 6.10 and 6.12 (chemical shifts in τ values);singlet at 3.05 (3-proton); doublet at 2.2 (J=9.5 cps) and a partly resolved quartet at about 3.41 (resorcinol pattern of the B-ring as in II); a signal at 3.5 overlapping with the high field part of the quartet of the 5'-proton (8- and 3'-

protons); and doublet at 3.67 (J=2.5 cps; 6-proton).

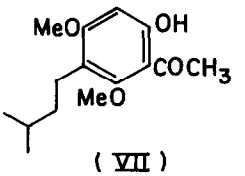
Artocarpesin was devoid of methoxyl groups as shown by the NMR spectrum; catalytic hydrogenation gave a dihydro-derivative, m.p. 252°. Both gave tetramethyl ethers (m.p. 148° and 158°), showing the presence of four hydroxyl groups. The UV spectrum (λ_{max}^{EtOH} 251, 271, 288sh., 355 mμ) of artocarpesin closely resembled the spectra of artocarpetin and norartocarpetin, revealing a similar oxygenation pattern and the absence of a substituent in the 3-position.

The NMR spectra of artocarpesin and dihydroartocarpesin were determined in DMSO and pyridine, and the methyl ethers in CCl_4. Artocarpesin shows three-proton signals with allylic coupling at 8.05 and 8.26 assigned to two methyl groups on C=CH; together with a doublet at 6.17 (J=7 cps; allylic and benzylic CH_2) which appears at 6.67 in the ether (the lower value of 6.17 being the solvent effect of pyridine), and a broad triplet at 4.76, they indicate a prenyl group attached to an aromatic ring.[7] This is confirmed by the absence in dihydroartocarpesin of the vinyl proton at 4.76 and the appearance of a six-proton doublet centred at 8.97 (J=5 cps) for an isopropyl group and two CH_2 triplets at 6.89 and 8.19, the former being benzylic. Artocarpesin therefore appeared to be 6- or 8-prenyl-norartocarpetin, probably the former by analogy with artocarpin and cycloartocarpin. The NMR spectrum of artocarpesin in the aromatic region showed five protons: sharp singlet at 2.97 (3-proton); single-proton doublet at 2.21 (J=9.5 cps) (6'-proton); a signal at 3.45 with a line width of 3 cps

(8-proton and doublet of 3'-proton); and a quartet partly merged with the 3.45 signal (5'-proton).



(VI)



(VII)

Structure (III) for artocarpesin was confirmed by synthesis of the tetramethyl ether of the dihydro-derivative by the selenium dioxide oxidation[8] of the chalcone (VI). The ketone (VII), condensation of which with 2,4-dimethoxybenzaldehyde gave (VI), was prepared by dibenzylation of isoamylphloracetophenone, methylation, debenzylation and monomethylation.

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