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PHENOLIC AND QUINOIDAL CONSTITUENTS OF DALBERGIA RETUSA

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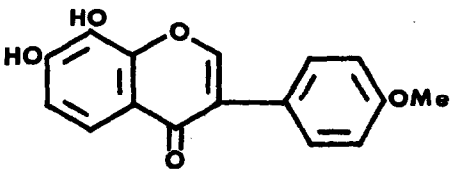
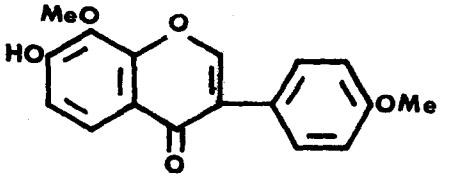
The heartwood of the Panamanian tree, Dalbergia retusa, is highly resistant to attack by marine borers[1]. The constituents of this species have not previously been identified, although those of a number of other Dalbergia species[2] have been the subject of numerous recent studies.

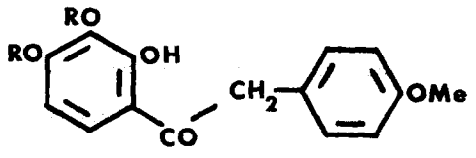
Ether extraction of Dalbergia retusa heartwood yields a colorless phenol (m.p. 249°; 1%), now called retusin and identified as 7,8-dihydroxy-4'-methoxyisoflavone I, and a second, colorless phenol, m.p. 221°, identified as 8-O-methylretusin II. These compounds appear to be the first 7,8,4'-trioxygenated isoflavones isolated from natural sources.



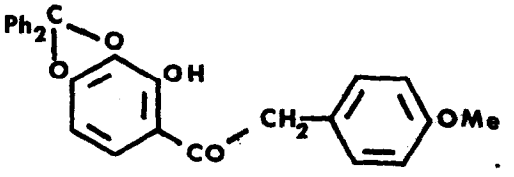
I



II



III



IV

a, R = H
b, R = Me

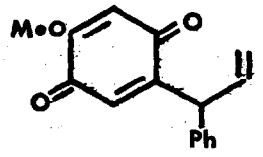
In accord with an isoflavone structure the UV spectrum of retusin has a single, high intensity peak at 261 nm (EtOH), and it forms a di-O-methyl derivative (m.p. 151°), which is hydrolyzed by EtOH-KOH to a deoxybenzoin IIIb. With HNO_3 retusin gave 3-nitroanisic acid. Retusin reduces $AgNO_3$, gives a green ferric reaction, and its $\lambda_{max.}$ shifts to 269 nm with boric acid/NaOAc. These data indicate ortho-orientation (3) of the two A ring hydroxyl groups; this being confirmed by the facile formation of a crystalline diphenylmethylene derivative of retusin with α,α-dichloro-

diphenylmethane. With NaOAc the $\lambda_{max.}$ of retusin shifts to 277 nm, locating (3) one OH at position 7. Since retusin is not identical with 6,7-dihydroxy-4'-methoxyisoflavone (texasin) (4), these data establish its structure as I. In accord with this proposal, the 100 MHz spectrum of its diacetate (m.p. 166°) shows the proton at C_2 as a singlet at δ7.94 and the protons at positions 3'(5'), 2'(6'), and 6 as ortho- coupled doublets (J = 9.0 Hz) at δ6.96, 7.47, and 7.25, respectively. The proton at C_5, ortho-to the carbonyl, occurs downfield as a doublet at δ8.20.

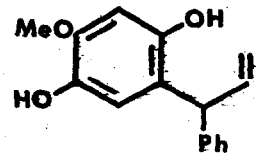
The structure of retusin was confirmed by synthesis. Alkaline hydrolysis of its diphenylmethylene derivative gave IV. Acid hydrolysis of IV gave a trihydroxy-deoxybenzoin identical with IIIa, synthesized (5) by condensation of pyrogallol with 4-methoxyphenylacetic acid. With ethyl orthoformate IIIa gave I, identical with the natural isoflavone.

The phenol, m.p. 221°, contains two OMe and one OH groups, and on methylation it gives di-O-methylretusin. The $\lambda_{max.}$ of this new isoflavone (256 nm) shifts to 270 nm with NaOAc, locating the OH at position 7, as in structure II. This structure was confirmed unambiguously by synthesis of II (identical with the natural product) and of the isomeric 8-hydroxy-4', 7-dimethoxyisoflavone (m.p. 203°). The $\lambda_{max.}$ of the latter did not shift with NaOAc.

D. retusa heartwood also yields a crystalline, orange pigment, $C_{16}H_{14}O_3$ (m.p. 178-179°; 3%) and smaller quantities of a blue-black, crystalline pigment, $C_{32}H_{30}O_6$ (m.p. 102-103°). The optically inactive, blue-black pigment is an easily dissociated molecular complex (quinhydrone) of an optically inactive, yellow quinone, $C_{16}H_{14}O_3$ (m.p. 125°), identical with racemic (6) methoxydalbergione V, and a colorless phenol, $C_{16}H_{16}O_3$ (m.p. 98°). NMR spectra of the phenol and of its diacetate (m.p. 104°) are in accord with structure VI (racemic obtusaquinol) and this was confirmed by the synthesis of the crystalline phenol by (a) sodium dithionite reduction of 4-methoxydalbergione V and of the natural quinhydrone, and (b) acid-catalyzed condensation (6) of methoxyquinol with cinnamyl alcohol. The co-occurrence of VI with V is interesting, because quinones and their corresponding quinols have rarely (7) been isolated from the same source. The occurrence of antipodes in the same plant is also rare (8), and racemic dalbergiones have not previously been isolated from plants (2). The synthetic quinhydrone, prepared by crystallizing equimolecular quantities of synthetic V and VI was identical in all respects with the product from D. retusa.

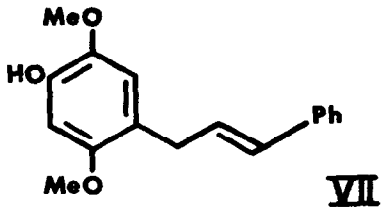


V

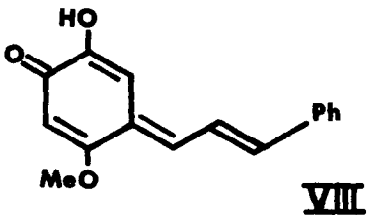


VI

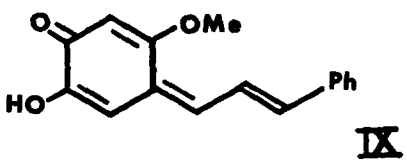
The orange pigment in Dalbergia retusa may be the principal protective constituent against marine organisms. It is highly toxic to fish, lethal concentrations being as low as 300 parts per billion for the species studied. The pigment has $\lambda_{max.}$ 397 nm, $\varepsilon_{max.}$ 37000 (EtOH), contains one OH and one OMe group, and its monomethyl derivative (m.p. 169°) is reduced to violastyrene VII by $NaBH_4$. The 100 MHz spectrum of the pigment in $CDCl_3$ shows OMe protons at δ3.85 (3H, S), uncoupled quinoidal protons at δ5.88 (1H, S) and δ6.83 (1H, S), and OH proton at δ6.96 (1H, S), and three ethylenic and five phenyl protons as an 8H multiplet at δ7.0-δ7.6. Reduction of the natural pigment yields o-diphenolic products, while PbO_2 or Ag_2O oxidation of synthetic violastyrene yields a pigment, $C_{17}H_{16}O_3$, m.p. 169°, identical (by m.m.p., TLC, NMR, and UV spectra) with the monomethyl derivative of the D. retusa pigment. These data indicate structure VIII or IX for the natural pigment, and eliminate the possible alternate structure X. Structure VIII or IX for the pigment was further confirmed by its synthesis by C-cinnamylation of 4-methoxycatechol and subsequent Ag_2O oxidation of the product. The synthetic pigment, m.p. 178-179°, was identical in all respects with the natural product.



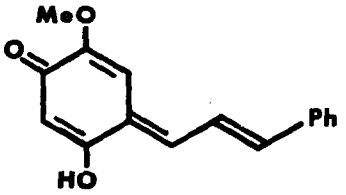
VII



VIII



IX



X

Both the synthetic and the natural pigment were readily reduced by sodium dithionite to a mixture of two o-diphenolic products. These observations established, therefore, that the D. retusa pigment is either identical in structure with obtusaquinone, a pigment isolated from Dalbergia obtusa[9] and briefly described in 1968, or is its geometrical isomer. Obtusaquinone was reported[9] to melt at 155° and to be stable to sodium dithionite reduction. These apparent anomalies have now been resolved by direct comparison* of the two pigments, which has confirmed their identity. The reported m.p. description of obtusaquinone should now be corrected* to read "m.p. 174-175°, with preliminary softening at 155-160°." We believe that chemical and spectral data do not allow unambiguous assignment of either geometric structure to this pigment. An attempt to differentiate these geometric isomers by X-ray analysis of the pigment and its monomethyl derivative is currently in progress in this Laboratory.

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* Private communication from W. D. Ollis.