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METABOLIC PRODUCTS OF P. HERQUEI

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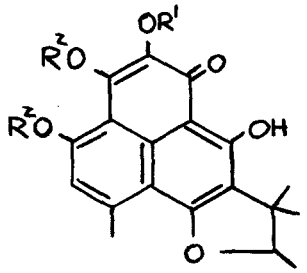
The recent report[1] that a new metabolite named herqueichrysin, isomeric with deoxyherqueinone (1; R^1= Me, R^2= H)[2] has been isolated from the mycelium of P. herquei grown in submerged culture prompts us to record our own work in this field. We also have isolated an isomer of deoxyherqueinone which affords a dimethyl ether, a trimethyl ether, and a triacetate, and although we have been unable so far to make a direct comparison it is clear from the physical properties reported for herqueichrysin and its triacetate that the metabolite isolated by us is identical with herqueichrysin. The IR, UV, and NMR spectra of herqueichrysin and its derivatives are characteristic of a phenalenone fused to a 1,2,2-trimethyldihydrofuran ring.[3] Since the material obtained by demethylation with pyridine hydrochloride is not identical with atrovenetin (1; $R^1 = R^2 = H$)[4] it follows that in the new metabolite the orientation of the ether ring must differ from that found in the other phenalenone-derived pigments of P. herquei.

The likeliest structure for the new metabolite appeared to us to be (2; one OH group methylated), which differs from atrovenetin only in that cyclisation of the isoprene side chain in the presumed precursor (3, or biosynthetic equivalent) implicates the phenolic hydroxy group at C_7 rather than that at C_9. In their recently published paper[1] Narasimhachari and Vining have also put forward (2) as the most probable structure for desmethylherqueichrysin on the basis of its spectra and acidity. We now report a synthesis of the compound (2) which, it transpires, is not identical with desmethylherqueichrysin.

A solution of the allyl ether (4; R = $CH_2CH{=}CMe_2$)[5] in dimethylformamide containing some added potassium carbonate was heated at 200° in a sealed tube for 4 hr. After a work-up procedure involving acidification with dilute hydrochloric acid, the phenalenone (5; R = H) (63%) and atrovenetin yellow trimethyl ether (1; $R^1 = R^2$ = Me) (15%) were isolated;

the latter compound was found to be formed readily by treatment of the phenalenone (5; R = H) with 2NHCl at room temperature for fifteen minutes. In order to prevent cyclisation to the atrovenetin ring system the 7-hydroxy group of compound (5; R = H) was blocked by methylation with diazomethane; treatment of the resulting methyl ether (5; R = Me) with dilute aqueous ethanolic hydrochloric acid then gave the cyclised product (6) (85%). Brief treatment with pyridine hydrochloride at 220° resulted in demethylation to give the tetrahydroxyphenalenone (2, or equivalent tautomer) (81%), the IR, UV, and NMR spectra of which differed from those recorded for desmethylherqueichrysin. Also, whereas the latter compound gave a tetra-acetate as the only major product of acetylation under mild conditions, compound (2), when similarly treated, afforded a mixture of a tri- and a tetra-acetate: the latter compound was not identical with desmethylherqueichrysin tetra-acetate. We shall defer further speculation concerning the structure of herqueichrysin until the completion of work which is in progress.



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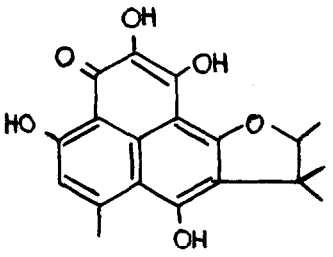

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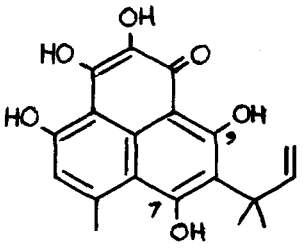

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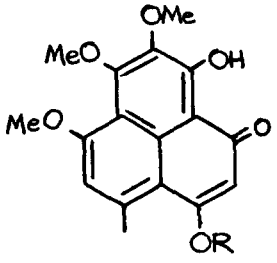

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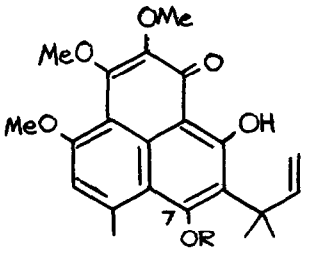

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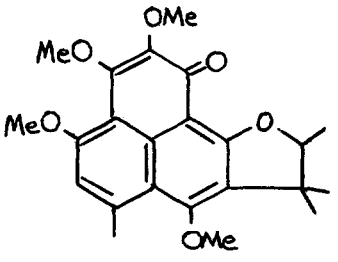

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In addition to herqueichrysin, herqueinone, isoherqueinone, norherqueinone, and isonorherqueinone we also isolated, from the mycelium of P. herquei grown in submerged culture,[6] atrovenetin (1; $R^1 = R^2 = H$) and deoxyherqueinone (1; $R^2 = Me$, $R^2 = H$). The possibility that under these culture conditions P. herquei gives rise to both (+)- and (-)-atrovenetin which serve as biosynthetic precursors for herqueinone and isoherqueinone respectively (through the appropriate enantiomer of deoxyherqueinone[7]) has already been mooted.[2b] In accordance with this view the atrovenetin isolated in the present work and its tri- and tetra-acetates have specific rotations of + 54.6°*, + 39.4°, and 18.3° respectively. Since the corresponding $[\alpha]_D$ values for R-(+)-atrovenetin and its acetates derived from P. atrovenetum are + 100.6°*, + 74.9°, and + 34°, the atrovenetin obtained from P. herquei has an optical purity of only 54%. Similarly the deoxyherqueinone isolated in the present work gave a diacetate, $[\alpha]_D$ + 43.6°, which corresponds to an optical purity of 53%, assuming a value of + 82° for the specific rotation of the pure enantiomer.[2b] Atrovenetin is stable to the conditions employed in extracting the mycelial products; while the occurrence of racemisation during the growth of the P. herquei is not excluded, the possibility remains that both (+)- and (-)-atrovenetin are metabolites of P. herquei.

Satisfactory analytical data and spectra were obtained for the new compounds described.

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* Dioxan solution: all other specific rotations refer to chloroform solutions.

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2. (a) J.S. Brooks and G.A. Morrison, Tetrahedron Letters, 1970, 963;
   (b) J. Chem. Soc. Perkin I, 1972, 421.
3. The data reported for herqueichrysin, its triacetate, and its desmethyl derivative in reference 1 are in good agreement with our own results; the spectra recorded for the methyl ethers of herqueichrysin are similar.

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5. D.A. Frost and G.A. Morrison, Chem. Comm., 1972, 93.

6. For culture conditions, see N. Narasimhachari, K.S. Gopalkrishman, R.H. Haskins, and L.C. Vining, Canad. J. Microbiol., 1963, 9, 134.

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