Lamellicolic Anhydride—a Heptaketide Naphthalic Anhydride from *Verticillium lamellicola*

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Summary The structure of lamellicolic anhydride from *Verticillium lamellicola* has been established using a number of transformations highly characteristic of the 2,7-dihydroxy-1,8-naphthalic anhydride system present, and by conversion into the naphthalic anhydride from *Penicillium herquei*.

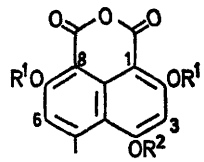
THE groups of fungal metabolites related to atrovenetin and to duclauxin appear to have in common a heptaketide skeleton[1] which is modified by prenylation in the former case and by dimerisation in the latter.[2] We report the isolation from a strain of the fungus *Verticillium lamellicola* (F. E. V. Smith) of a number of metabolites which are based on the simple heptaketide skeleton.†

Broth extracts of *V. lamellicola* have weak antibacterial and antifungal activity[3] due to the presence of traces of an antibiotic which as yet has not been identified. Close to this in polarity (but virtually inactive) was the major metabolite, lamellicolic anhydride (I), R_F 0·35 in MeOH–$CHCl_3$ (1:9), which formed yellow needles from MeOH–$CHCl_3$, decomposing over 300°, $C_{13}H_8O_6$ (M^+ at 260·0323). The solubility of this in aqueous sodium hydrogen carbonate, its twin i.r. absorption at 1700 and 1650 cm^{-1}, and complex u.v. spectrum apparently showing a reversible hypsochromic shift on basification are all characteristic of the 1,8-naphthalic anhydride system present in (I).[4] The presence in (I) of three phenolic OH groups was indicated by the formation of the tri-*O*-acetyl derivative (II), m.p. 177—179° and tri-*O*-methyl derivative (III), m.p. 290° (decomp.), ν_{max} 1750, 1715 cm^{-1}.

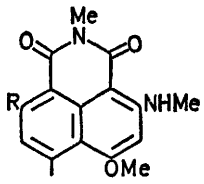
Aryl methoxy-groups *peri* to carbonyl groups are often readily cleaved by magnesium iodide–etherate[5] and with this reagent, (III) afforded the monomethoxy-derivative (IV), m.p. 260° (decomp.), also obtained as a minor product in the methylation of (I). Treatment of (III) with hot aqueous methylamine confirmed the presence of the chelated anhydride system in a remarkable manner, the aminoimides (V), m.p. 225—228°, and (VI), m.p. 244—246°, being formed (NH resonances at τ −1·5 and −0·3, respectively).

The environments of the aryl protons in (I) and (III) were confirmed by the detection of 6-H–*C*-Me coupling and, in the latter case, by nuclear Overhauser effects. Thus in CF_3CO_2H the signal at τ 2·73 (6-H) was enhanced 21 and 11% per irradiation at τ 6·94 (*C*-Me) and 5·73 (*O*-Me), respectively, while the signal at τ 3·14 (3-H) was enhanced 0 and 37, respectively, by irradiation at the same frequencies. Successive treatment of (I) with aqueous NaOH

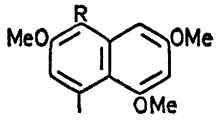
† Biosynthetic evidence in support of this assertion will be reported elsewhere.



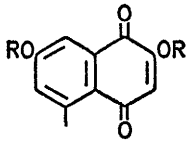
(I) $R^1 = R^2 = H$
(II) $R^1 = R^2 = Ac$
(III) $R^1 = R^2 = Me$
(IV) $R^1 = H, R^2 = Me$



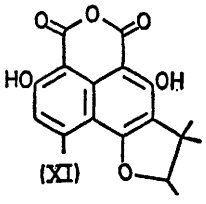
(V) R = NHMe
(VI) R = OMe



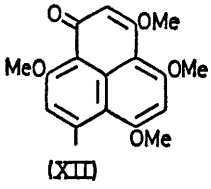
(VII) $R = CO_2Me$
(VIII) R = H



(IX) R = H
(X) R = Me



(XI)



(XII)

(N$_2$) and diazomethane gave (VII), m.p. 126—128°, and (VIII), m.p. 93—95°, in which the new aryl protons introduced by decarboxylation could be seen to be *meta* coupled (J 3 Hz) to the appropriate proton originally present. If, after treatment of (I) with alkali, the solution was allowed to stand in air, the orange quinone (IX), m.p. 250° (decomp.) was obtained.[6] The 8-H proton appeared in the n.m.r. spectrum of the corresponding dimethyl ether (X), m.p. 172—173°, as a doublet (J 2 Hz) at τ 2·42, and the singlet corresponding to 3-H (τ 3·9) showed substantial enhancement upon irradiation at *ca.* τ 6·1 (OMe). The quinone (IX) was also isolated from the broth extracts. As yet we have been unable to disprove that this is formed naturally, at least to some extent, during the fermentation process.

The evidence summarised above conclusively establishes the structure of lamellicolic anhydride (I) and this has been confirmed by conversion into the anhydride (XI),[7] a sample of which was prepared from herqueinone[8] provided by Professor R. Thomas. Conclusive proof has been provided independently[9] by synthesis of (III) and (I) *via* the tetramethoxyphenalenone (XII).[10] Two minor metabolites closely related to (I) will be discussed elsewhere.

All new compounds gave the requisite spectral and analytical data.

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[3] U.K. Patent Application No. 36,963/1954.
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