A New Fungal Tetrahydrofuran

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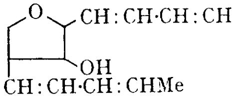
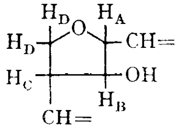
A METABOLITE, $C_{13}H_{18}O_2$, m.p. 64°, has been isolated from culture filtrates of *Chaetomium coarctatum* and identified as 2-(buta-1,3-dienyl)-3-hydroxy-4-(penta-1, 3-dienyl)tetrahydrofuran (I).



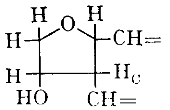
(I)

The infrared spectrum of the compound shows hydroxy-group absorption at 3300—3150 cm.$^{-1}$ but no strong absorption between 2000 and 1200 cm.$^{-1}$. Its ultraviolet spectrum [λ_{max}235 mμ (ϵ 53,300) (in MeOH)] is evidence, therefore, of a bis-diene part-structure. The n.m.r. spectrum (in $CDCl_3$ with added D_2O) shows a three-proton doublet at τ 8·27 ($:C\cdot CH_3$), a one-proton quintuplet at τ 7·20 ($:C\cdot CH$), four one-proton triplets at τ 5·5–6·5 ($H\cdot C\cdot O\cdot$), and a nine-proton complex between τ 3·5 and 5·0 ($:C\cdot H$). When measured in dimethyl sulphoxide, the n.m.r. spectrum shows an additional one-proton doublet at τ 4·68 (removed by adding D_2O), characteristic of a secondary alcohol.[1]

Catalytic reduction of the compound gives a product, m.p. 35—36°, shown by mass spectrometry to be an octahydro-derivative (*M* 214) and by n.m.r. to contain no olefinic protons and only two methyl groups (τ 8·9—9·3). This must mean that the diene chromophores are present as the substituents $CH_2:CH\cdot CH:CH\cdot$ and $CH_3\cdot CH:CH\cdot CH:CH\cdot$. The remaining $C_4H_6O_2$ is necessarily monocyclic, and, since only one proton is α to the hydroxyl group, three protons must be α to the other oxygen. Two alternative part-structures, (II) and (III), suggest themselves at this point, both involving the tetrahydrofuran ring.



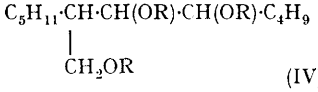
(II)



(III)

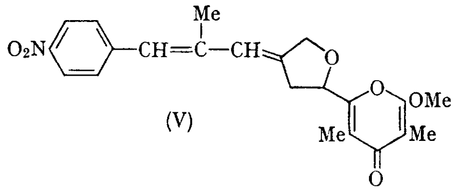
Double-irradiation experiments at 100 Mc./sec. provide convincing support for (II). Spin-decoupling of the allylic proton (H_C in both cases) causes three of the four triplets in the τ 5·5—6·5 region to be replaced by doublets, a result in agreement with (II) but eliminating (III) as a possibility. H_A is presumably responsible for the triplet furthest down-field, and H_B must correspond to the triplet which, broad in deuterochloroform, sharpens on addition of deuterium oxide. That the relevant coupling constants are similar is support for both assignments. Simultaneous irradiation of H_A and one of the protons H_D converts the H_C quintuplet into a quartet. So does irradiation at 536 c./sec., which must therefore saturate an olefinic proton α to H_C. Similarly, irradiation at 553 c./sec. reduces the signal from H_A to a doublet, proving that it, too, is coupled to olefinic hydrogen.

Whereas the mass spectrum of the unsaturated compound reveals little apart from the appropriate molecular weight, that of the octahydro-derivative allows one to decide between the two possible arrangements of the diene side-chains in (II). The initial fragmentation involves loss of either 57 or 71 units, the C_4H_9 or C_5H_{11} side-chains. Of the associated peaks, the one at 157 is far larger than that at 143, and this is evidence for placing the shorter side-chain α rather than β to the ether oxygen. This assignment was confirmed as follows. Reaction of the octahydro-derivative with acetic anhydride and zinc chloride (*cf.* ref. 2) gave a mixture of stereoisomeric triacetates (IV; R = Ac), which was hydrolyzed with barium

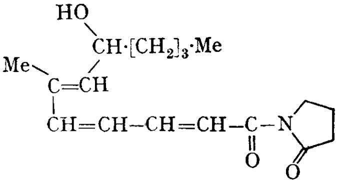


$$\underset{\displaystyle CH_2OR}{C_5H_{11}\cdot CH}\cdot CH(OR)\cdot CH(OR)\cdot C_4H_9$$

(IV)



(V)



(VI)

hydroxide solution to the corresponding triols (IV; R = H). Periodate oxidation of the vicinal diol grouping then present was shown to give n-pentanal rather than n-hexanal as a major product.

Few fungal tetrahydrofurans are known. The substitution pattern in this new member of the class, also observed in aureothin (V),[3] would seem to call for a branched precursor, and, in fact, the carbon skeleton required is exactly reproduced in the revised structure for variotin (VI).[4]

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[1] O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, 1964, **86**, 1256.
[2] O. Grummitt, J. A. Stearns, and A. A. Arters, *Org. Synth.*, Coll. Vol. III, 1955, 833.
[3] Y. Hirata, H. Nakata, K. Yamada, K. Okuhara, and T. Naito, *Tetrahedron*, 1961, **14**, 252.
[4] S. Takeuchi, H. Yonehara, and H. Shoji, *J. Antibiotics (Japan)*, 1964, *A*, **17**, 267.