The Molecular and Crystal Structure of a Derivative of Ophiobolin-D

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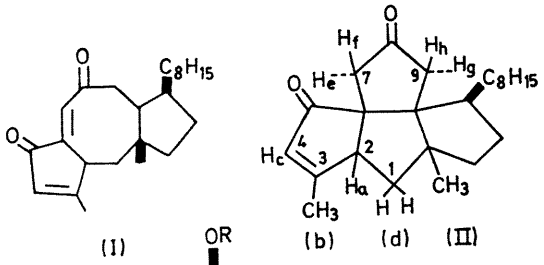
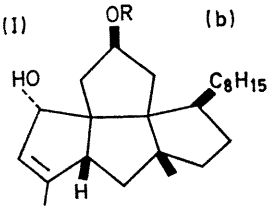
Summary A derivative of ophiobolin-D has a structure which contains a novel ring system consisting of four fused five-membered rings.

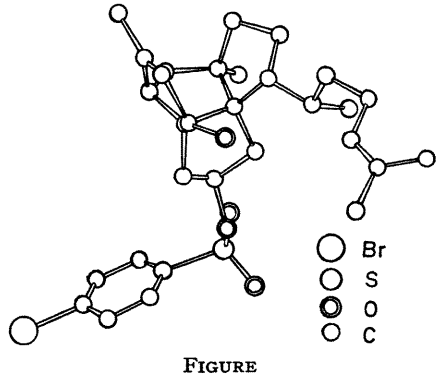
DEHYDRO-OPHIOBOLIN-D, a derivative of a fungal metabolite,[1] was easily decarboxylated by heating to just above





(III) R = H
(IV) R = $OSO_2C_6H_4Br$

its melting point to afford compound (I), along with two isomeric products.[2] Treatment of (I) with a trace of potassium t-butoxide in t-butyl alcohol gave quantitatively



FIGURE

the product (II), m.p. 92°, ν_{max} 1743 cm^{-1} (saturated five-membered-ring ketone). A deuterium exchange experiment showed the presence of nine exchangeable hydrogens, and a β-methyl $\alpha\beta$-unsaturated five-membered-ring ketone system was indicated by i.r. (1696, 1622 cm^{-1}), n.m.r. (δ, 2·04, 5·75) and u.v. (λ_{max} 236 nm) measurements. Double-resonance experiments revealed that the signal at δ 3·11 (H_a, br t) coupled with the C-3 methyl[3] protons (H_b, δ 2·07), 4-H proton (H_c, δ 5·75), and the adjacent methylene protons (H_d, δ 1·80); J 1·3, 1·9, and 9·0 Hz, respectively. Two pairs of AB quartets due to the methylene protons at C-7 and C-9 appeared at δ 2·80, H_e: δ 2·42, H_f (J 19·5 Hz) and δ 2·575, H_g: 2·325, H_h (J 18 Hz). Long-range coupling between H_e and H_g (J 1·2 Hz) and H_f and H_h (J 1·7 Hz)

was observed. Upon irradiation at the tertiary methyl signal (δ 0·95), a nuclear Overhauser effect was observed for H_h (about 5—8% increase).

The results indicate that the product has the structure (II), which might be formed by transannular cyclisation between C-6 and C-10. Inspection of a molecular model suggests that all ring junctions are *cis*. Formation of the new bond could be explained on the basis of intramolecular Michael attack of a carbanion produced at C-10 by prototropic shift to C-2.

The structure and the stereochemistry of the compound (II) were confirmed by single-crystal *X*-ray diffraction studies of a heavy-atom derivative. Treatment of the diol (III), which was obtained by lithium aluminium hydride reduction of the diketone (II), with *p*-bromobenzenesulphonyl chloride afforded the mono-*p*-bromobenzenesulphonate (IV), m.p. 88°, $C_{30}H_{41}O_4SBr$. The retention of the original carbon skeleton in (IV) was shown by a comparison of its spectral properties with those of (III) and by the fact that the diol (III) was converted into the starting diketone (II) with Jones' reagent.

The crystals of (IV) are monoclinic, space group $P2_1$ and the lattice parameters are $a = 10{\cdot}17$, $b = 8{\cdot}56$, $c = 16{\cdot}75$ Å, and $\beta = 90{\cdot}25°$. A total of 1265 independent reflections were collected from multiple-film equi-inclination Weissenberg photographs and the structure was solved by the heavy-atom method. Several calculations of the structure factors and electron density maps gave the whole structure. A view of the molecule is shown in the Figure. Structure parameters were refined by the block-matrix least-squares method. The final *R* value was 9·5%.

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