Crystallographic Studies of Fusicoccin and Two Mercuribromide Derivatives

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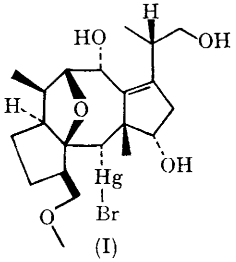
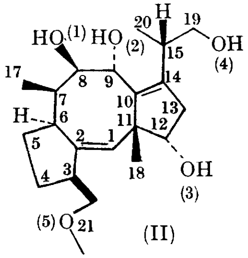
ATTEMPTS to determine the structure of fusicoccin by *X*-ray analysis have proceeded simultaneously with the chemical studies summarised in the two adjoining Communications.[1,2] Fusicoccin was found to crystallize from a variety of solvents (methanol, benzene, or acetone–light petroleum) with slightly differing habits, but all having essentially the same unit cell and space group (monoclinic, $P2_1$, $a = 20{\cdot}7$, $b = 14{\cdot}4$, $c = 13{\cdot}5$ Å, $\beta = 96{\cdot}6°$) containing 4 molecules of fusicoccin ($C_{36}H_{56}O_{12}$) per cell (*i.e.* 2 molecules per asymmetric unit) and varying levels of solvation which made them unreliable for molecular weight determination. We found it possible to incorporate bromobenzene, iodobenzene, *m*-dibromobenzene, and bromothiophen into this lattice with only trivial changes of cell dimensions, but the heavier solvate molecules never exceeded 25% molar concentration compared to fusicoccin. The magnitude of the task of solving and refining such a structure and the absence of information about rigid groups in this molecule dissuaded us from further work on solvated crystals.

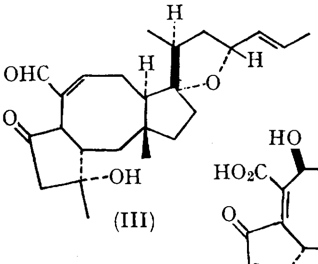
The first usable heavy-atom derivatives obtained were two mercuribromides. The first, made from fusicoccin, surprisingly still contained the vinyl group. It was monoclinic, $C2$, $a = 11{\cdot}37$, $b = 9{\cdot}42$, $c = 42{\cdot}62$ Å, $\beta = 97{\cdot}37°$, $D_m = 1{\cdot}4$, $D_c = 1{\cdot}42$ g.cm.$^{-3}$ for 4 molecules of $C_{36}H_{55}O_{12}HgBr$ per cell. The second was made from the desacetyl aglycone and crystallized as tetragonal prisms, space group $I4$, $a = 19{\cdot}550$, $c = 13{\cdot}375$ Å, $D_m = 1{\cdot}63$, $D_c = 1{\cdot}68$ g.cm.$^{-3}$ for 8 molecules of $C_{21}H_{33}O_5HgBr$ per cell. As these were much the better quality crystals, had lower thermal attenuation and also seemed slightly less vulnerable to *X*-radiation damage, they were studied first. Intensity data for 2520 reflexions were recorded with Cu-K_α radiation on an automatic diffractometer for a succession of six crystals. The solution and refinement of the structure has been straightforward; *R* is currently 0·100.



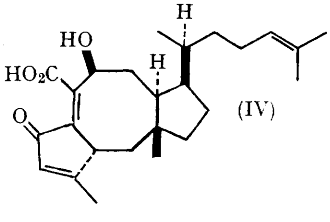
(I)



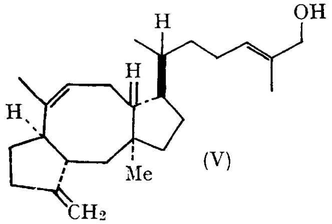
(II)



(III)



(IV)



(V)

The molecule has the constitution and relative stereochemistry (I) shown in the Figure. From this we deduce the desacetyl aglycone to be (II) and Barton *et al.*,[2] have been able to propose a structure for fusicoccin A. The addition of the mercury atom and the bridging of the 8-membered ring O(1) take place easily and constitute a *trans*-attack on the double-bond C(1)=C(2). Exactly the same mode of substitution-*cum*-bridging has been shown by Barton *et al.*[2] to occur in the mercuribromide of fusicoccin.

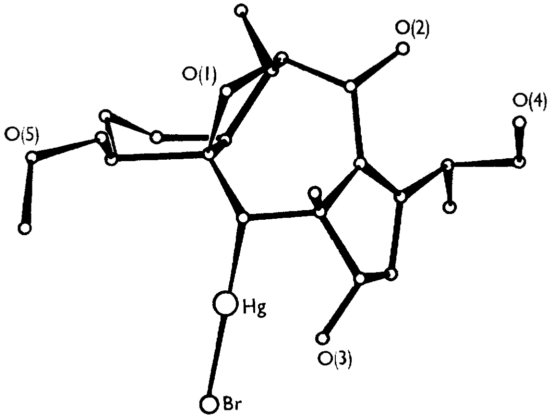


FIGURE. c-*Axis projection of mercuribromide of fusicoccin desacetyl aglycone.*

The carbocyclic skeleton, although a diterpene, has only previously been found in the sesterterpenes,[3-6] and the presence of the fifth isoprene unit attached to the glucose suggests that this latter may at some stage in the biogenesis have been joined to a sesterterpene by two ether bridges. *X*-Ray structures and absolute configurations have been reported for three sesterterpenes: ophiobolin A (cochliobolin) (III),[3] ophiobolin D (cephalonic acid) (IV),[4] and ceroplastol (V).[5] Ophiobolins A and D are also fungal metabolites and also phytotoxic (though having only about 5% the potency of fusicoccin) whereas ceroplastol is an insect product. The absolute configuration of our mercuribromide is being determined by *X*-ray fluorescence to permit effective comparison with the above sesterterpenes, and also to establish which enantiomer of the aglycone has to be linked to D-glucose.

Addendum: While these three communications were being prepared an elegant *X*-ray determination of the structure of the iodobenzenesulphonate of fusicoccin appeared with supporting chemistry.[7] This is in full accord with our proposal for the constitution and relative stereochemistry of the aglycone.

Comparison of the 8-membered ring before and after cyclisation shows that relief of non-bonded repulsions on C(17) exerted by C(4), C(5), and C(16) may facilitate bridging, and so may help account for the ease and stereospecificity of this reaction and the preference of mercury for this double bond rather than for the vinyl group.

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[2] K. D. Barrow, D. H. R. Barton, E. B. Chain, U. F. W. Ohnsorge, and R. Thomas, following Communication.

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[7] A. Ballio, M. Brufani, C. G. Casinovi, S. Cerrini, W. Fedeli, R. Pellicciari, B. Santurbano, and A. Vaciago, *Experientia*, 1968, **24**, 631.