The Constitution and Absolute Stereochemistry of Verrucarin A

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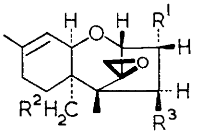
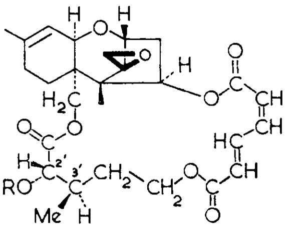
RECENTLY there has been considerable interest in a number of closely related sesquiterpene alcohols of type (I), some obtained directly as metabolic products, and others obtained by hydrolysis of metabolic products, of diverse fungi. The constitution and relative stereochemistry of trichodermin, isolated from a *Trichoderma* species, was established as (I; $R^1 = R^2 = H$, $R^3 = OAc$) by *X*-ray analysis of trichodermol *p*-bromobenzoate.[1] Since trichodermol (I; $R^1 = R^2 = H$, $R^3 = OH$) is identical with roridin C, a minor metabolic product of *Myrothecium roridum*, Godtfredsen and Vangedal concluded[2] that verrucarol, the sesquiterpenoid hydrolysis product of the antibiotic verrucarin A[3] which is also a product of *M. roridum*, must have structure (I; $R^1 = H$, $R^2 = R^3 = OH$) rather than the structure proposed earlier by Tamm.[4] This revised formula was supported by further degradative studies by Tamm and his colleagues.[5] Subsequently, the structure (I; $R^1 = OH$, $R^2 = R^3 = OAc$) was assigned by two independent groups[6,7] to diacetoxyscirpenol, the principal phytotoxic metabolic product of *Fusarium equiseti*.[8]



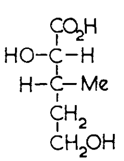
(I)

With the structure, apart from absolute configuration, of verrucarol settled Tamm was able from further degradative studies to deduce structure (II; R = H) for verrucarin A; by the isolation of the acids (III) and IV) the absolute stereochemistry at positions-2′ and -3′ was established but these positions were not correlated with the asymmetric centres of the verrucarol moiety.[9]

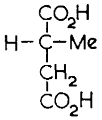
We have subjected verrucarin A *p*-iodobenzenesulphonate to crystal-structure analysis and our results unambiguously define the constitution and absolute stereochemistry at all asymmetric centres of the derivative as (II; $R = O_2SC_6H_4I$). It follows that verrucarin A is correctly represented in constitution and absolute stereochemistry by (II; R = H) and that the absolute configurations of the compounds (I) are as indicated. We are informed by Professor Ch. Tamm that applications of Horeau's rules[10] (to which exceptions are known) to verrucarol and trichothecolone are consistent with our findings.



(II)

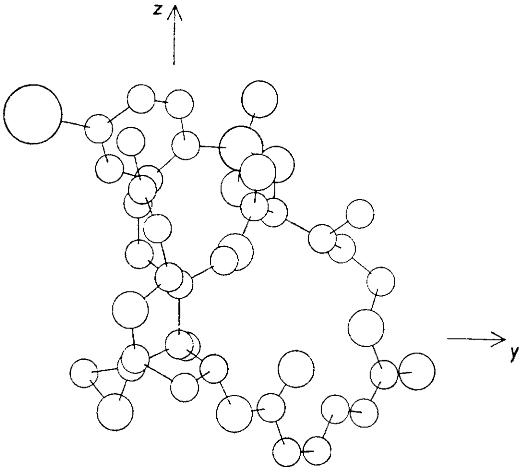


(III)



(IV)

Verrucarin A *p*-iodobenzenesulphonate crystallizes from acetone as an acetone solvate, the crystals of which belong to the orthorhombic system, space group $P2_12_12_1$, with four units of $C_{33}H_{37}O_{11}SI$, C_3H_6O in a cell of dimensions $a = 17{\cdot}98$, $b = 19{\cdot}66$, $c = 10{\cdot}65$A. Three-dimensional *X*-ray intensity data were recorded on equi-inclination



The arrangement of atoms within one molecule of verrucarin A p-*iodobenzenesulphonate, as viewed along the* a *axis of the crystal.*

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[1] S. Abrahamsson and B. Nilsson, *Proc. Chem. Soc.*, 1964, 188.

[2] W. O. Godtfredsen and S. Vangedal, *Proc. Chem. Soc.*, 1964, 188.

[3] E. Härri, W. Loeffler, H. P. Sigg, H. Stähelin, Ch. Stoll, Ch. Tamm, and D. Wiesinger, *Helv. Chim. Acta*, 1962, **45**, 839.

[4] J. Gutzwiller and Ch. Tamm, *Helv. Chim. Acta*, 1963, **46**, 1786.

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[7] A. W. Dawkins, J. F. Grove, and B. K. Tidd, *Chem. Comm.*, 1965, 27.

[8] P. W. Brian, A. W. Dawkins, J. F. Grove, H. G. Hemming, D. Lowe, and G. L. F. Norris, *J. Exp. Bot.*, 1961, **12**, 1.

[9] J. Gutzwiller and Ch. Tamm, *Helv. Chim. Acta*, 1965, **48**, 157.

[10] A. Horeau, *Tetrahedron Letters*, 1961, 506; 1962, 965; *Tetrahedron*, 1964, **20**, 2431.

Weissenberg photographs and estimated visually; in all 2126 independent $|F_0|$ values were derived. The atoms, apart from hydrogen, were located in three-dimensional electron-density distributions. The atomic co-ordinates were subsequently refined by the least-squares method and the value of R is now 12·8%. The iodine and sulphur atoms were assigned anisotropic temperature factors, but the carbon and oxygen atoms were assigned only isotropic values in order to conserve computer time. The absolute configuration was deduced by Bijvoet's anomalous-dispersion method.[11]

The arrangement of atoms within the molecule of verrucarin A *p*-iodobenzenesulphonate as viewed along the *a* axis of the crystal is shown in the Figure.

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