Crystal Structure and Absolute Configuration of Wortmannin and of Wortmannin *p*-Bromobenzoate

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Summary The crystal structure and absolute configuration of the fungal metabolite Wortmannin, isolated from *Myrothecium roridium Tode ex Fries*, have been determined.

WORTMANNIN, $C_{23}H_{24}O_8$ (I) was first isolated by Brian *et al.*[1] from *Penicillium Wortmanni*. In the adjoining communication,[2] Macmillan *et al.* have established the constitution by chemical methods. We report here the crystal structures of both the native compound (I) and the *p*-bromobenzoate (II) together with the absolute configuration derived from measurements of the effects of anomalous scattering in the latter compound. The material was isolated from *Myrothecium roridium Tode ex Fries*.

Crystal data: Wortmannin, $C_{23}H_{24}O_8$, $M = 428$, orthorhombic, $a = 2567(7)$, $b = 702(1)$, $c = 1177(2)$ pm, $U = 2119{\cdot}4 \times 10^6$ pm^3, $D_m = 1{\cdot}34$, $Z = 4$, $D_c = 1{\cdot}34$, space group $P2_12_12_1$ (D_2^4, No. 19).

Wortmannin *p*-bromobenzoate, $C_{30}H_{26}BrO_9$, $M = 610$, monoclinic, $a = 1337(3)$, $b = 2925(4)$, $c = 738(1)$ pm, $\beta = 97{\cdot}31(5)°$, $U = 2862 \times 10^6$ pm^3, $D_m = 1{\cdot}43$, $Z = 4$, $D_c = 1{\cdot}42$, space group $P2_1$ (C_2^2, No. 4).

Intensity data for both compounds were collected on a Hilger and Watts Linear diffractometer, employing graphite monochromatised Mo-K_α radiation; 1781 and 3005 measurements respectively yielded 1331 and 1324 significant reflections with $I \geqslant 3\sigma(I)$. The heavy atom derivative was solved first, but because of problems arising from insufficient data, and a non-crystallographic two-fold screw axis relating the steroid fragments of the two independent molecules, refinement was terminated at $R = 0{\cdot}13$ and hydrogen atoms were not located. At this time, good crystals of the native compound became available, and the structure could readily be determined by multi-solution direct methods. Refinement was carried out by block-diagonal least-squares, using anisotropic vibrations for C and O and isotropic for H, to a present R of 0·04. An isotropic extinction parameter[3] was also refined. The absolute configuration was established to be that shown in the Figures by an R factor ratio test[4] on (II) (significant at the 0·005 level) and a series of measurements of Friedel pairs on a Nonius Kappa-diffractometer.†

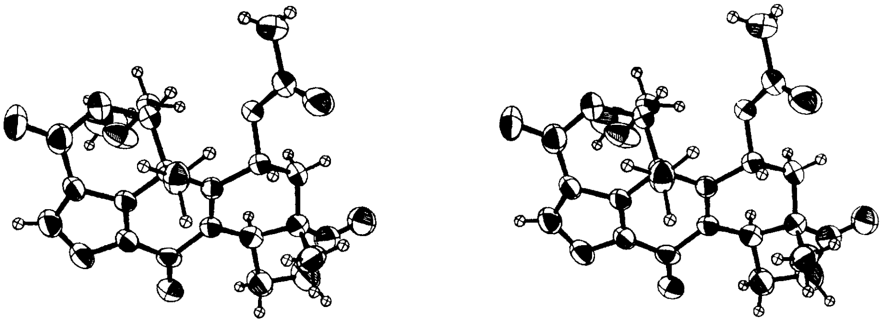


FIGURE 1. *Stereopair of the Wortmannin molecule.*

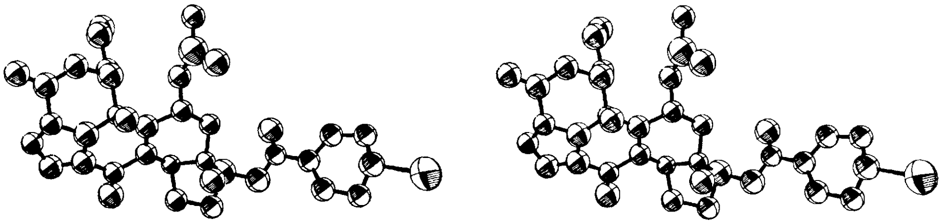
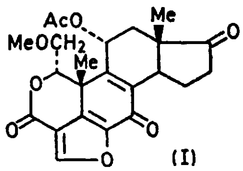
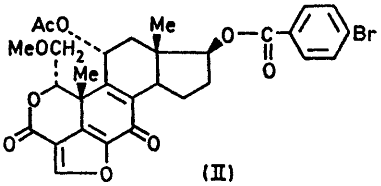


FIGURE 2. *Wortmannin* p-*bromobenzoate* (*molecule A*) *from the same viewpoint as in Figure* 1.

Figure 1 shows the conformation of Wortmannin and Figure 2 that one of the two independent molecules of the *p*-bromobenzoate. The other molecule has the same conformation with the exception of the torsion angle



(I)



(II)

between the D-ring and the *p*-bromobenzoate group. The only conformational difference observed between (I) and (II) is in the methoxymethyl substituent at position 1.

In Wortmannin, the chain C(10)–C(1)–CH_2–O–Me is *synclinal-antiplanar*, whereas in both molecules of the parabromobenzoate, this chain is *antiplanar-antiplanar*. In Wortmannin, the A-ring is in the twist (C_2) conformation, with C(10) 42 pm above and C(1) 32 pm below the plane of O(2)–C(3)–C(4)–C(5) (standard stereoidal numbering). Ring B is a flattened envelope, with C(10) 12 pm out of the mean plane, and rings C and D (*trans*-junction) are also in envelope conformations with C(13) and C(14) the flaps respectively. Ring E is absolutely planar (all torsion angles zero) but is not coplanar with the B-ring. There is a dihedral angle of 12·3° between them.

Viridin[5], which has the same fused ring system A/B/E, shows a similar distortion of the C(5)–C(6) double bond, but the B-ring is more in a flattened boat conformation.

(*Received*, 31*st July* 1972; *Com.* 1332.)

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† We thank Dr. Littke, of the University of Freiburg-im-Breisgau for making this facility available to us.

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