X-Ray Determination of the Molecular Structure of a Derivative of Dothistromin, a Fungal Toxin Implicated in Pine Needle Blight

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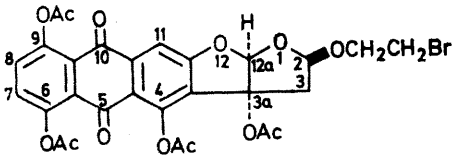
Summary An *X*-ray diffraction study of a derivative of the red fungal toxin dothistromin reveals a molecular structure in which two fused furan rings are joined to a trihydroxyanthraquinone moiety: the absolute configuration has been established.

INVESTIGATIONS into the organism responsible for "pine-needle blight," a disease first identified in commercial pine forests in New Zealand in 1964, have led to the isolation of the fungal pathogen, *Dothistroma pini*, and subsequently to the extraction of a red toxin, of stoicheiometry $C_{28}H_{22}O_9$, named dothistromin.[1] To establish configurations at asymmetric centres we have undertaken an *X*-ray diffraction study of the acetylated bromoethyl ether.

Data were collected by automatic diffractometry using Mo-K_α radiation: $a = 6{\cdot}050(3)$, $b = 38{\cdot}194(16)$, $c = 12{\cdot}204(5)$ Å, space group $P2_12_12_1$, $Z = 4$. The present *R*-factor, for a model which includes hydrogen atoms, is 0·141. The molecular structure (Figure), has three asymmetric centres with the absolute configurations indicated. (This result is specified by 80% of those Friedel pairs which have an intensity difference $\geqslant 10\%$). It is seen to contain a triacetoxyanthraquinone moiety joined to a *cis*-fused difuran system and is formally 2,3,3a,5,10,12a-hexahydro-2-(2-bromoethoxy)-3a,4,6,9-tetra-acetoxy-5,10-dioxoanthra[2,3-*b*]furo[3,2-*d*]-furan. The molecule thus contains the difuro-group found earlier in the aflatoxins,[2] the sterigmatocystins,[3] and the versicolorins.[4]

Molecular bond-lengths and angles are as expected, as is the overall planarity of the basic skeleton with the obvious exceptions dictated by the *cis*-fusion of the five-membered rings.



Dothistromin itself is the pentahydroxy-parent of the derivative but possible epimerisations at asymmetric centres make uncertain a complete stereochemical correlation between the two. Racemisation is not likely to have occurred at the benzyl hydroxy-group of C-3a, nor is it likely that anything but *cis*-fusion takes place between the furan rings, so two configurations remain unchanged. The ready epimerisation which can be expected at C-2 precludes specification of this centre in the parent toxin. There is also the possibility that scission at C-12–C-12a followed by ring-closure involving the OH group at C-4 would lead to an isomerism between the "linear" molecule revealed by this study and an "angular" one.[1] This would not, however, lead to a change in configuration at C-12a since *cis*-fusion of the rings ensures that the stereochemistry is dictated by C-3a. The configuration at these two asymmetric centres, as determined for dothistromin tetra-acetate and thus for dothistromin itself, is the same as that deduced for aflatoxins by degradative studies.[5]

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