X-Ray Structure of Viridicatumtoxin: A New Class of Mycotoxin from *Penicillium viridicatum* Westling

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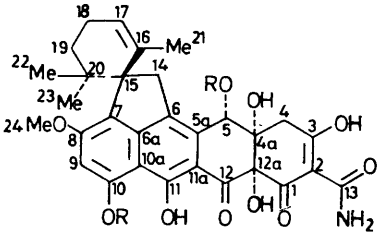
Summary The structure of viridicatumtoxin, the main toxin of strains of *Penicillium viridicatum* Westling has been established as (**1a**) by *X*-ray methods; the toxin is structurally related to the tetracyclines.

THE renal toxins oxalic acid, citrinin,[1] and ochratoxin A[2] are known metabolites of *Penicillium viridicatum*. However, cultivation of toxigenic strains of *P. viridicatum* (C.S.I.R. 1029) on sterilized maize meal yielded none of the known mycotoxins and only a new toxin, viridicatumtoxin, was isolated.[3]



(1)
a; R = H
b; R = COMe

Viridicatumtoxin (**1a**), $C_{30}H_{31}NO_{10}$, crystallised from MeOH, m.p. 235 °C (decomp.), containing one mole of solvent of crystallisation. It had $[\alpha]_D^{23} - 12°$ (*c* 1·0, EtOH); λ_{max} (EtOH) 237, 285, 317, 331, 347, and 424 nm (log ϵ 4·34, 4·51, 3·44, 3·40, 3·28, and 3·90 respectively), ν_{max} ($CHCl_3$) 3550—3350, 2980, 1725, 1650, 1620, and 1595 cm^{-1}. The high-resolution mass spectrum was uninformative and showed strong peaks only at *m/e* 565 (M^+), 548 ($M^+ - NH_3$), 529 ($M^+ - 2H_2O$), 509 ($M^+ - C_4H_8$), and 492 [$M^+ - (C_4H_8 + NH_3)$], each associated with a metastable peak.

With only the preceding information as to the structure, a single-crystal *X*-ray structure determination was carried out. The yellow crystals are monoclinic prismatic, space group *A*2 (No. 5) with $a = 12·979(1)$, $b = 7·832(1)$, $c = 30·148(2)$ Å, $\beta = 105·44(1)°$, $Z = 4$. *X*-Ray intensity data for 3136 reflections were collected on a Nonius CAD4 diffractometer. The structure was determined by direct methods applying a quartet invariants approach.[4] All but one of the hydrogen atoms of the toxin were found and included in the calculation and the structure has been refined to an *R*-factor of 0·053. The absolute configuration of the toxin is not known as yet although a determination will be attempted later using the anomalous scattering of

oxygen. An ORTEP[5] drawing, assuming the known configuration of tetracycline, is given in the Figure.

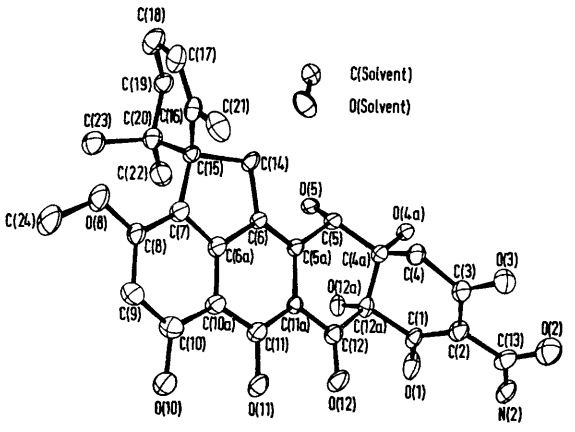


FIGURE. ORTEP drawing of the molecular conformation of viridicatumtoxin (**1a**).

Individual bond lengths and angles agree well with the accepted values and those reported for 5,12a-diacetoxytetracycline.[6] The spiro cyclohexene ring has a half-chair conformation. The ^1H and ^{13}C n.m.r. spectra are consistent with structure (**1a**). Further details of the X-ray structure will be reported later.

Derivation and degradation of (**1a**) gave mostly intractable mixtures. However, treatment of (**1a**) with acetic anhydride–sodium acetate gave 5,10-diacetylviridicatumtoxin (**1b**), $C_{34}H_{35}NO_{12}$, m.p. 219—221 °C, from bromobenzene. Its n.m.r. spectrum showed δ 2·36 (10-OAc) and 2·18 (5-OAc). The C(9) proton appeared at δ 6·86 [δC(9) 109·0 p.p.m.] and the C(5) proton at δ 6·18 [δC(5) 70·5 p.p.m.] in (**1b**) compared to the C(9) proton at δ 6·62 [δC(9) 100·12 p.p.m.] and the C(5) proton at δ 4·48 [δC(5) 71·56 p.p.m.] in (**1a**).

Viridicatumtoxin is structurally related to the tetracyclines, a group of broad-spectrum antibiotics produced by *Streptomyces* spp. A novel feature of (**1a**) is the spiro arrangement of the two isoprenoid units to form the additional two rings. The production of a tetracycline derivative by micro-organisms other than the *Streptomyces* is of chemotaxonomic importance. A tetracycline derivative[7] and demethylchlorotetracycline[8] have been reported to cause photosensitivity in humans. It is, therefore, of importance to note that Butiarso *et al.*[9] observed that rice cultures of *P. viridicatum* induced a hepatogenous phototoxic syndrome in mice upon exposure to sunlight; a possible role of (**1a**) in this primary photosensitization syndrome requires further investigation.

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