X-Ray Crystal Structure of Asteltoxin, a Novel Mycotoxin from *Aspergillus stellatus* Curzi

By GERT J. KRUGER, PIETER S. STEYN, and ROBERT VLEGGAAR*

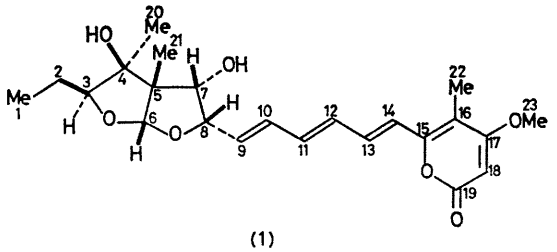
(*National Chemical Research Laboratory, Council for Scientific and Industrial Research, P.O. Box* 395, *Pretoria* 0001, *Republic of South Africa*)

and CHRISTIAAN J. RABIE

(*National Research Institute for Nutritional Diseases, Medical Research Council, Tiervlei* 7505, *Republic of South Africa*)

Summary The structure of a new mycotoxin, asteltoxin, isolated from cultures of *Aspergillus stellatus* is proposed, based on ^{13}C and ^{1}H n.m.r. spectral data and *X*-ray crystallography.

THE investigation of toxic maize meal cultures of *Aspergillus stellatus* Curzi (MRC 277) led to the isolation of a novel mycotoxin, asteltoxin, for which the structure (**1**) (or its enantiomer) is proposed. The mycotoxin (**1**) crystallized from acetone as small, pale yellow needles, m.p. 130—132 °C, and analysed for $C_{23}H_{30}O_7$, (M^+ 418·1984); $[\alpha]_D^{23}$ + 20·0° (*c* 1·15, MeOH). The u.v. spectrum, λ_{max} (MeOH) 367, 272·5, and 267 nm (ϵ 32,760, 29,360, and 29,260), was similar to that of aurovertin B (**2**).[1] The i.r. spectrum of (**1**) showed absorptions at 1680, 1620, and



(1)

1530 cm^{-1} (KBr) consistent with the presence of an α-pyrone unit. Structural evidence in favour of structure (**1**) for asteltoxin was deduced mainly from its ^{13}C and ^{1}H n.m.r. spectra. The assignments are summarized in the Table.

TABLE. N.m.r. data for asteltoxin. Chemical shifts in p.p.m. relative to Me_4Si

	^{13}C N.m.r.[a]	^{1}H N.m.r.[b]	*J*/Hz
C(1)	10·8Q	1·05t	7·5
C(2)	21·7T	1·55m	
C(3)	89·3D	4·30dd	6·0; 7·0
C(4)	80·2S	—	
C(5)	61·9S	—	
C(6)	112·3D	5·28s	
C(7)	79·4D	3·70dd	3·0; 5·0
C(8)	84·0D	4·75m	
C(9)	120·2D	5·87dd	5·0; 15·0
C(10)	131·8D*	[c]	
C(11)	132·4D*	[c]	
C(12)	133·0D*	[c]	
C(13)	137·1D*	7·20dd	11·0; 15·5
C(14)	134·9D*	[c]	
C(15)	154·1S	—	
C(16)	107·9S	—	
C(17)	161·9S	—	
C(18)	88·6D	5·50s	
C(19)	170·3S	—	
C(20)	15·7Q†	1·19s	
C(21)	17·6Q†	1·38s	
C(22)	8·1Q	1·95s	
C(23)	56·0Q	3·83s	

*† These assignments may be interchanged.

[a] Taken in $(CD_3)_2CO$ on a Varian CFT-20 spectrometer at 20·0 MHz. [b] Taken in $CDCl_3$ on a Bruker WP-200; C(7)-OH: δ 1·81 (d, *J* 5 Hz), C(4)-OH: δ 1·6 br. [c] Complex multiplet δ 6·25—6·75.

A single-crystal *X*-ray study was undertaken in order to confirm the structure (**1**) for asteltoxin. Suitable crystals, although of poor quality, were obtained by crystallization from methanol. The yellow crystals were monoclinic, space group $P2_1$ (no. 4) with $a = 9{\cdot}341(5)$, $b = 15{\cdot}641(9)$, $c = 8{\cdot}963(5)$ Å, $\beta = 106{\cdot}64(4)°$, $Z = 2$, and included methanol of crystallization ($C_{23}H_{30}O_7.CH_3OH$). Intensity measurements were made with Mo-K_α radiation ($\lambda = 0{\cdot}7107$ Å; graphite monochromator) on a Philips PW 1100 four-circle diffractometer to $\theta = 22°$. A total of 1559 unique reflections were measured, of which 142 were regarded as unobserved with $I < \sigma(I)$. The structure was solved by direct methods and refined by least-squares techniques using the SHELX computer program.[2] Hydrogen atoms were included at calculated positions with a common isotropic temperature factor. During refinement the hydrogen atom co-ordinates were constrained to maintain constant bond lengths and appropriate bond angles. The hydroxy-proton co-ordinates were not refined. The final *R*-factor with anisotropic temperature factors for all nonhydrogen atoms and using $1/\sigma_F^2$ weights was 0·105. The resulting structure is illustrated in the Figure.‡ In the crystal the hydrogen bonds O(3)-H · · · · (methanol) · · · · O(2) and O(4)-H · · · · O(6) link neighbouring molecules into infinite chains along the *z*-direction.

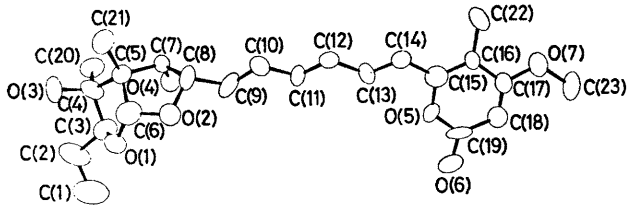
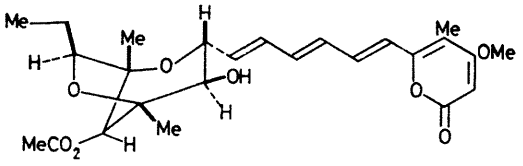


FIGURE. Perspective drawing of asteltoxin.

Asteltoxin (**1**) is structurally related to citreoviridin (**3**)[3] and the aurovertins, *e.g.* aurovertin B (**2**),[1] both potent inhibitors of ATP-synthesis and ATP-hydrolysis catalysed by mitochondrial enzyme systems.[4] Biosynthetic studies have shown that citreoviridin is derived from a C_{18}-polyketide precursor.[5] The overall structures of aurovertin B (**2**) and asteltoxin (**1**) are consistent with a polyketide



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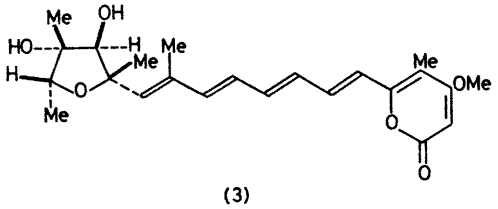

(3)

origin. However, if the two compounds originated from a C_{18}-polyketide, C(1) must be derived by introduction of a methyl group from the C_1-pool on the methyl carbon of the chain-initiating acetate unit. Alternatively, a C_{20}-polyketide origin requires the loss of the methyl carbon of the chain-initiating acetate unit. There is no firmly established precedent in polyketide biosynthesis for either of these processes. Furthermore, in the biosynthesis of asteltoxin a rearrangement of the polyketide chain must be invoked to explain the formation of the bistetrahydrofuran unit. A similar rearrangement occurs in the biosynthesis of the aflatoxins and sterigmatocystin.[6] The presence of the isolated bistetrahydrofuran unit in asteltoxin is unique amongst fungal metabolites.

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‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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