Toxic 12,13-Epoxytrichothec-9-enes from *Fusarium* sp.

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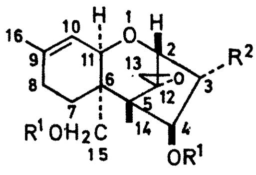
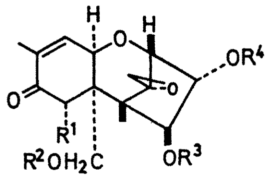
Summary The structures and absolute configurations of a number of compounds obtained from a group of closely-related *Fusarium* sp. have been determined by correlation with 4β,15-diacetoxy-12,13-epoxy-trichothec-9-en-3α-ol (diacetoxyscirpenol).

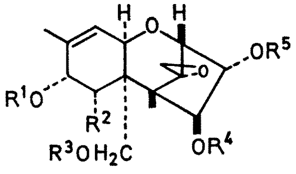
THE naturally-occuring esters of the group of sesquiterpene alcohols containing the tetracyclic 12,13-epoxytrichothec-9-ene nucleus[1] constitute an important class of mycotoxins.[2] The structure and absolute configuration of diacetoxyscirpenol (I; R^1 = Ac, R^2 = OH) have been established[3,4] by relating it to verrucarol (I; R^1 = R^2 = H), whose absolute configuration is known.[5] A number of these toxic compounds have now been related to diacetoxyscirpenol and their structures and absolute configurations thereby determined.



(I)



(II)



(III)

Structure (II; R^1 = OH, R^2 = R^3 = Ac, R^4 = H) was assigned,[6] mainly on spectroscopic evidence, to the $C_{19}H_{24}O_9$ diacetate from *F. scirpi*;[7] that this also represents the absolute configuration follows[8] from the direct conversion of the enone (II; $R^1 = H$, $R^2 = R^3 = R^4 = Ac$) into the diacetyl-derivative (II; $R^1 = OAc$, $R^2 = R^3 = R^4 = Ac$) of (II; $R^1 = OH$, $R^2 = R^3 = Ac$, $R^4 = H$) by acetoxylation with lead tetra-acetate. The enone (II; $R^1 = H$, $R^2 = R^3 = R^4 = Ac$) has been obtained from diacetoxyscirpenol by acetylation and oxidation with t-butyl chromate[4] and from the acetylated 8α-(3-methylbutyrloxy)-derivative (III; $R^1 = Me_2CH{\cdot}CH_2{\cdot}CO$, $R^2 = R^5 = H$, $R^3 = R^4 = Ac$)[9,10] by oxidation with selenium dioxide.[9]

Partial hydrolysis of the diacetate (II; $R^1 = OH$, $R^2 = R^3 = Ac$, $R^4 = H$) gave the 4β-monoacetate (II; $R^1 = OH$, $R^2 = R^4 = H$, $R^3 = Ac$), identical with fusarenone.[11] Hydrolysis of both ester groups furnished the parent tetraol (II; $R^1 = OH$, $R^2 = R^3 = R^4 = H$), identical with nivalenol.[12] The exceptional lability of the ester groups of (II; $R^1 = OH$, $R^2 = R^3 = Ac$, $R_4 = OH$), attributed to participation by the neighbouring 7α- and 3α-hydroxy-substituents, suggests that both fusarenone and nivalenol may be artifacts derived by hydrolysis of the diacetate during the lengthy isolation procedures.[11,12]

Reduction of the 8-oxo-group of the diacetate (II; $R^1 = OH$, $R^2 = R^3 = Ac$, $R^4 = H$) with sodium borohydride took place from the less crowded β-face to give the 3α,7α,8α-triol (III; $R^1 = R^5 = H$, $R^2 = OH$, $R^3 = R^4 = Ac$). The diacetyl derivative (III; $R^1 = R^3 = R^4 = R^5 = Ac$, $R^2 = OH$) was identical with a monoacetyl-derivative of the $C_{21}H_{28}O_{10}$ triacetate from *F. scirpi*[7] which (n.m.r.) has structure (III; $R^1 = R^3 = R^4 = Ac$, $R^2 = OH$, $R^5 = H$).[8]

All the naturally-occurring biologically-active trichothecanes contain an ethylenic double bond at C-9 and a 12,13-epoxy-group. The elucidation of the structures of the toxins based on (II; $R^1 = OH$) and (III; $R^2 = OH$) illustrates the remarkable capacity of some Fusaria for oxidation of the trichothecane nucleus, which is mevalonate-derived.

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