5-Methoxysterigmatocystin, a Metabolite from a Mutant Strain of *Aspergillus versicolor*

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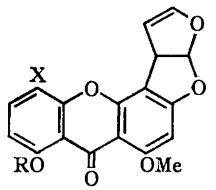
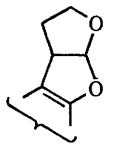
A new metabolite, $C_{19}H_{14}O_7$, has been isolated from a strain of *Aspergillus versicolor* produced by irradiation of wild-strain spores. The structure of this metabolite followed from a comparison of the n.m.r. spectrum with that of sterigmatocystin (I).[1] These were similar except that the former compound showed an additional OMe signal and a different pattern in the aromatic region. Thus, the new metabolite had two *o*-coupled aromatic protons at τ 3·29 and 2·82 (J 10·0 c./sec.) together with a singlet aromatic proton at 3·57, whereas sterigmatocystin showed three coupled aromatic protons in addition to a similar singlet. This evidence together with considerations of chemical shift values strongly suggested that the new compound is 5-methoxysterigmatocystin (II). Confirmation was provided by a synthesis of the dihydro-derivative (IV) from dihydrosterigmatocystin (V). Oxidation of the latter compound by the Elbs persulphate reaction gave the 5-hydroxy-derivative (VI)[2] from which the 5-*O*-methyl ether (IV) was generated by monomethylation with dimethyl sulphate and potassium carbonate in acetone. This was identical with the

product prepared by hydrogenation of the new metabolite.



	R	X
(I)	H	H
(II)	H	OMe
(III)	Ac	OMe

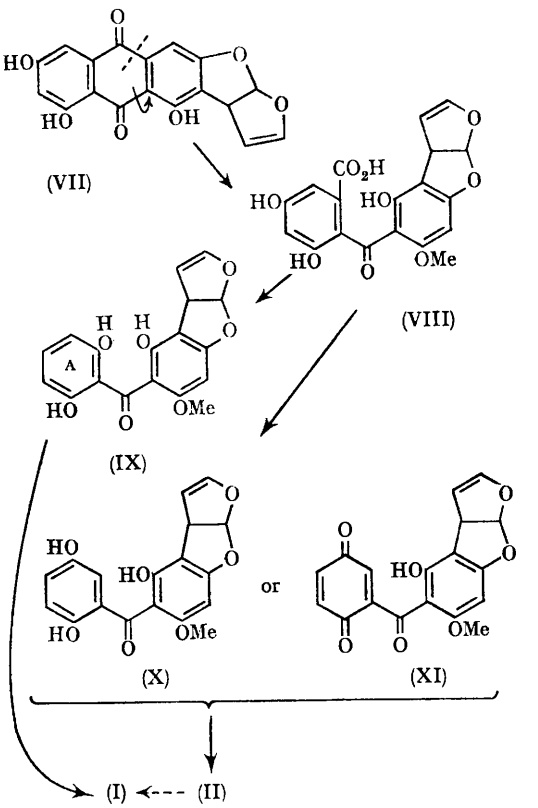


	R	X
(IV)	H	OMe
(V)	H	H
(VI)	H	OH

A metabolite, claimed to be 6-methoxysterigmatocystin, has been isolated from a strain of *A. versicolor*.[3] Comparison of the m.p.s and infrared spectra of this compound† and 5-methoxysterigmatocystin strongly suggested that the two were identical. This view was confirmed by a direct comparison of the derived *O*-acetates (III).*

The mutant which produces 5-methoxysterigmatocystin does not produce significant quantities of sterigmatocystin, whereas the wild strain from which it was derived produced relatively large quantities of sterigmatocystin and only traces of the 5-methoxy-derivative. Hence, it seems probable that the latter compound is either a biological precursor of the former, or that both are derived from a common intermediate, *e.g.*, 5-hydroxysterigmatocystin.

The co-occurrence of sterigmatocystin and the anthraquinone versicolorin A (VII)[4] in certain strains of the organism suggests that the xanthone may be biologically derived from an anthraquinone or related anthrone precursor in a manner similar to that suggested for the ergochromes.[5] The Scheme outlines the possible transformations involved. Initially, oxidative fission would give a benzophenone acid [type (VIII)] in which subsequent cyclisation would involve either dehydration of a hydroxylated intermediate [type (IX)] or oxidative coupling *via* radical or quinone intermediates.[6] In the latter case it would be necessary to introduce an additional



oxygen function into ring A of the benzophenone (VIII), *ortho* or *para* to the coupling position. In intermediates (X) and (XI) this is illustrated by an *o*-oxygen function. The natural occurrence of 5-methoxysterigmatocystin (II) and hence of the likely 5-hydroxy-precursor suggests that the biogenetic origin of the xanthone involves oxidative coupling, rather than cyclodehydration of a benzophenone intermediate.

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