Tetrahedron Letters No. 32, pp 2765 - 2766, 1977. Pergamon Press. Printed in Great Britain.

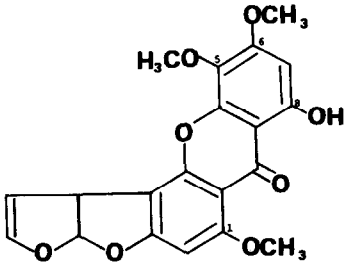
5,6-DIMETHOXYSTERIGMATOCYSTIN, A NEW METABOLITE FROM *ASPERGILLUS MULTICOLOR*

Takashi Hamasaki, Takeo Nakagomi, Yuichi Hatsuda,
Faculty of Agriculture, Tottori University, Koyama, Tottori, Japan
Keiichi Fukuyama, and Yukiteru Katsube
Faculty of Engineering, Tottori University, Koyama, Tottori, Japan

(Received in Japan 23 May 1977; received in UK for publication 20 June 1977)

In the course of our investigation of fungal metabolites we have isolated a new metabolite containing a bisdihydrofuran ring system from mycelial mats of *Aspergillus multicolor* Sappa together with sterigmatocystin and averufin. We wish to report the structure of the new metabolite.

The metabolite (I), $C_{20}H_{16}O_8$, was crystallized from acetone to give pale yellow needles, mp 253-254°C, $[\alpha]_D^{20}$ -363° (c=1.0, $CHCl_3$), *m/e* 384 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3125, 1655, 1635, 1610. UV λ_{max}^{EtOH} nm (ε): 233(27200), 248(34000), 275sh(7700), 330(19200). Its UV spectrum is closely similar to that of sterigmatocystin. In the NMR spectrum of I in $CDCl_3$ signals at δ 4.80(1H, d.d.d, J=2, 2.5 and 7 Hz), 5.41(1H, d.d, J=2 and 2.5 Hz), 6.46(1H, d.d, J=2 and 2.5 Hz) and 6.75 (1H, d, J=7 Hz) showed the presence of a bisdihydrofuran ring system in I. Three methoxyl signals were observed at δ 3.91, 3.94 and 3.98. Two singlet signals at δ 6.28(1H) and 6.32(1H) were assignable to the aromatic protons of xanthone nucleus. Hydrogenation of I gave a dihydro-derivative (II), mp 241-242°C. In the NMR spectrum of I a singlet signal at δ 13.20 was assignable to the hydrogen-bonded proton of phenolic hydroxyl group. Acetylation of I gave a monoacetate (III), mp 188-189°C. Methylation of I gave a monomethyl ether (IV), mp 257-258°C. Demethylation of II gave a dihydroxy-derivative (V), mp 238-240°C, whose NMR spectrum showed two singlet signals at δ 11.90 and 12.18 assignable to the protons of hydrogen-bonded hydroxyl groups. Alkaline degradation of I with 15% potassium hydroxide in ethanol gave a hydroxy-xanthone (VI), mp 221-222°C. Its NMR



(I)

spectrum showed three signals at δ 7.15(1H, m), 7.66(1H, m) and 8.17(1H, m) assignable to the protons of β-substituted furan ring. Methylation of VI gave a dimethyl ether (VII), mp 225-226°C. An aromatic proton at δ 6.32 in I showed downfield shift (0.18 ppm) on acetylation of the hydroxyl group. This is characteristic of the proton *ortho* to a phenolic hydroxyl group.

The locations of three methoxyl groups and the bisdihydrofuran ring in I were inferred from NMR spectra. Three methoxyl signals of I in C_6D_6 showed upfield shift (δ 3.20, 3.25, 3.73). Two strongly shifted signals at δ 3.20 and 3.25 were assignable to the protons of methoxyl groups *ortho* to the aromatic protons. In the NMR spectrum of IV a newly appeared methoxyl group signal at δ 3.93 in $CDCl_3$ was shifted upfield by 0.43 ppm in C_6D_6; this shift value agreed with that reported for 8-*O*-methylsterigmatocystin.[1] This fact indicates the presence of a hydroxyl group at the position 8 in I. These support that a hydroxyl group locates on an aromatic nucleus not bearing the bisdihydrofuran ring system. In the NMR spectrum of VII in C_6D_6 the upfield shifted four methoxyl signals were observed at δ 3.18(3H), 3.25(3H) and 3.46(3Hx2). Based on the above-mentioned data, the assumed structure (I) is deduced to the metabolite.

The structure of monoacetate (III) has confirmed by a single-crystal X-ray analysis. The crystals were monoclinic, space group C2, with Z=4 in a cell of dimensions a=19.76, b=5.09, c=20.41 Å, β=105.7°. The structure was solved by Patterson and Fourier methods and refined by least-squares method to R=0.135.

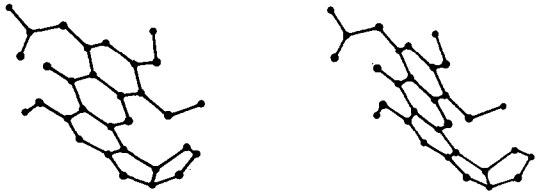


Fig. 1

A stereoscopic view of monoacetate (III) is shown in Fig.1. The two assymmetric centers in figure are based on absolute configuration of *p*-bromobenzoate of sterigmatocystin.[2]

The authors wish to thank Mr. Norio Nakajima for the assistance of X-ray analysis, and Mr. Isao Tanaka and Prof. Tamaichi Ashida of Nagoya University for their permission to use the computer programs.

References

1) P.S.Steyn and R.Vlegaar, *Jour. Chem. Soc. Perkin. I*, 1974, 2250.

2) K.Fukuyama, T.Tsukihara, Y.Katsube, N.Tanaka, T.Hamasaki, and Y.Hatsuda, *Bull. Chem. Soc.*, (Japan) 48, 1980(1975).