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FUMIGATONIN, A NEW MEROTERPENOID FROM ASPERGILLUS FUMIGATUS

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Summary: The structure of fumigatonin, a new meroterpenoid isolated from Aspergillus fumigatus IFM 4482 was elucidated by X-ray analysis.

Previous investigation of metabolites of Aspergillus fumigatus IFM 4482 resulted in the isolation of fumitremorgins[1] and tryptoquivalines[2]. We now wish to report the structure of fumigatonin, a new metabolite having a novel structure from this fungus.

Fumigatonin was isolated from a fraction obtained by silica gel column chromatography eluted with $CHCl_3$-methanol(30:1). Fumigatonin, mp 250-253°C (colorless needles from methanol), $C_{29}H_{38}O_{11}$, showed $[\alpha]_D^{17}$ +44° (c=0.877, methanol); MS m/z(%) 562(M^+,1), 213(100), 43(over); λmax(ethanol) 219(ε 10000) nm; νmax(KBr) 1797, 1738, 1716 cm^{-1}. These data and the ^1H- and ^{13}C-NMR spectra suggested that fumigatonin contains a highly oxidized and complicatedly condensed ring system. The detailed structure as well as the relative stereochemistry of this compound was established by X-ray analysis.

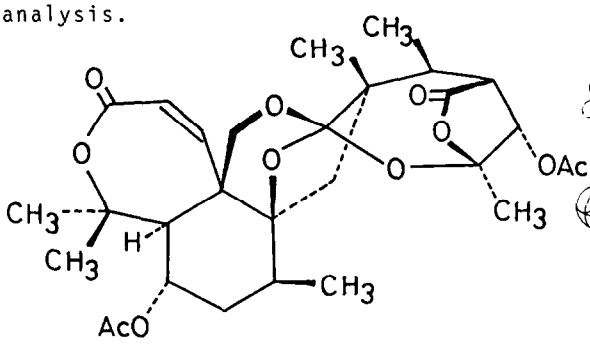
Crystals of fumigatonin were obtained from tetrahydrofuran: triclinic, space group P1, a=10.104(7), b=9.804(17), c=9.186(19) Å, α=116.77(18), β=95.83(11), γ=97.19(11)°, V=793.1 $Å^3$, Dc=1.33 g/cm^3, Z=1, included tetrahydrofuran of crystallization ($C_{29}H_{38}O_{11}\cdot C_4H_8O$). The intensity data of 2726 indpendent reflections ($I>2\sigma I$) with $2\theta \geqq 130°$ were collected on an automatic four-circle diffractometer with graphite-monochromated CuKα radiation. The structure was solved by direct method. Block-diagonal least-squares refinement with anisotropic temperature factors for the non-hydrogen atoms except the atoms of tetrahydrofuran and with isotropic temperature factors for the non-hydrogen atoms of tetrahydrofuran and hydrogens except methyl and tetrahydrofuran to give a final R value of 0.078. For additional crystallographic details consult reference 3. The structure obtained by X-ray analysis is supported by various spectra.

Fumigatonin seems to be a meroterpenoid such as paraherquonin[4] from

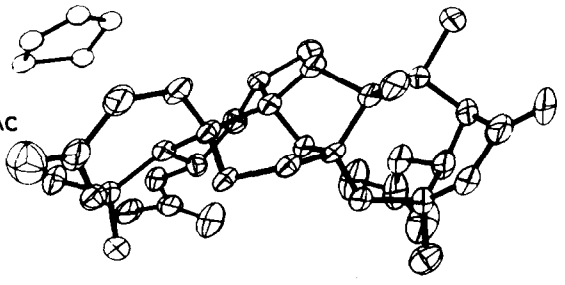
Penicillium paraherquei, austinol[5] and dehydroaustinol[6] from Emericella dentata, austin[7] from Aspergillus ustus, terretonin[8] from Aspergillus terreus and andilesins and andibenins[9] from Emericella variecolor. The biogenesis of fumigatonin was speculated to be formed by a novel variations of the same key intermediate which was derived from farnesylpyrophosphate and a bis-C-methylated tetraketide as well as these meroterpenoids.[10]

Some of meroterpenoids (austin, terretonin etc.) have been reported as mycotoxin. Fumigatonin, however, has shown no lethal effect by the intraperitoneal injection of 100 mg/kg to mice.

We acknowledge the help of Dr.K.Hamada for the refinement of X-ray analysis.



Structure of Fumigatonin



Computer Generated Perspective Drawing of Fumigatonin

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