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FOMANNOXIN - A TOXIC METABOLITE OF FOMES ANNOSUS

Masao Hirotani[1], Joseph O'Reilly and Dervilla M. X. Donnelly,*
Department of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland
Judith Polonsky,
Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette, France

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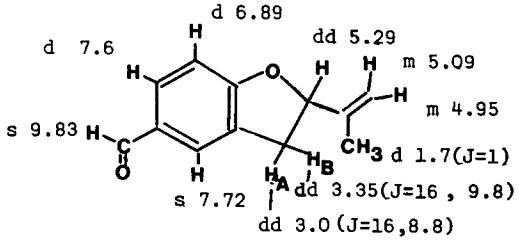
Fomes annosus is one of the relatively few Basidiomycete fungi that cause death of host cells in living trees, as well as extensive decay in heartwood of diseased trees. Previous phytochemical studies have shown that the volatile hexa-1,3,5-triyne[2] is emitted by the fungus and that oxalic acid[3] and fomannosin[4] are secreted when the fungus is grown on a culture medium. The sesquiterpene fomannosin is reported to be a phytopathogen[4a]. Concurrent with a biosynthetic study on the fomannosin[5], a detailed phytochemical investigation of the metabolites of the fungus was undertaken. We report the isolation from the culture broth of a dihydrobenzofuran with a toxicity to Chlorella pyrenoidosa[6] that is 100 times greater than that of fomannosin. It is proposed to name the benzofuran fomannoxin.

Fomannoxin (I) an oil $C_{12}H_{12}O_2$ (m/e M^+ found: 188.0827, calc. 188.0837) had the following physical and spectroscopic properties: $\{\alpha\}_D^{21^o}$ + 88.8° (c 0.144, $CHCl_3$), λ_{max}(MeOH)nm(log ε) 206 (4.43) 229 (4.37) 282(sh) (4.36) 293 (4.37); ν_{max}($CHCl_3$) cm^{-1} 1685, 1610; PMR ($CDCl_3$, TMS) δ 1.77 (3H, d, J 1.0Hz, Me) 3.0 (1H, dd, J 16, 8.8Hz, 3-H_A) 3.35 (1H, dd, J 16, 9.8Hz, 3-H_B) 5.29 (1H, dd, J 8.8, 9.8Hz, 2-H) 4.95, 5.09 (2H, m, = CH_2) 7.6, 6.89 (2H, 2d, J 8.9Hz, 6-,7-H) 7.72 (1H, s, 4-H) 9.83 (1H, s, -CHO).



In spin decoupling experiments, irradiation at δ 3.24 reduces the dd at δ 5.29 to a singlet whilst irradiation at δ 5.29 causes collapse of the octet for the methylene at C_3 to an AB quartet at δ 3.24. Fommanoxin, which is unstable, was reduced with $NaBH_4$ to give the 5-carbinol as an oil (Found: C, 75.51; H, 7.33. $C_{12}H_{14}O_2$ requires C, 75.75; H, 7.42%). $[\alpha]_D^{21^o}$ + 20.8° (c 0.26, $CHCl_3$); CD (c, 0.01, CH_3OH) $[\theta]_{285}$ - 2311; $[\theta]_{233}$ + 14230; λ_{max}(MeOH)nm(log ε) 208 (4.01) 233 (3.94) 282 (3.56) 290(sh) (3.52); ν_{max}($CHCl_3$) cm^{-1} 3620. PMR ($CDCl_3$); δ 1.79 (3H, d, J 1.0Hz, Me) 2.21 (1H, s, OH, exchanges D_2O) 3.01 (1H, dd, J 15.9, 8.8Hz, 3-H_A) 3.42 (1H, dd, J 15.9, 9.2Hz, 3-H_B) 4.6 (2H, s, -CH_2O.) 5.23 (1H, dd, J 8.8, 9.2Hz, 2-H) 4.98, 5.24 (2H, s(br)x2, =CH_2) 7.2, 6.8 (2H, 2d, 6, 7-H) 7.26 (1H, s, 4-H). Besides fomannosin and fomannoxin the culture broths contained at least three other metabolites which are currently being investigated. To date only ergosterol peroxide[7] was isolated from the mycelium. A survey has shown that Fomes annosus (obtained from widely different locations and hosts) grown in culture, produces either fomannosin or fomannoxin as the major metabolite[8]. Work is in progress to confirm the biosynthetic pathway for the dihydrobenzofuran (I) and to consider its possible role as a vivotoxin.

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References and Notes

1. Present address: Department of Pharmacognosy and Phytochemistry, Kitasato University, 9-1 Shirokane 5-chome, Minato-Ku, Tokyo, Japan.

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8. Ten strains of F. annosus were examined. All strains produced both fomannosin and fomannoxin.