PRUBTULOSIN, AN ANTIBIOTIC METABOLITE OF STEREM PRUBTULOSUM

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A yellow crystalline compound isolated in small amounts from culture liquids of the basidio-mycete, Stereum frustulosum, was antibiotic toward several types of microorganisms: In serial dilution tests, it was active against Staphylococcus aureus, Bacillus mycoides and B. subtilis at a concentration of 16 ppm and against several fungal species at somewhat higher concentrations. It was also moderately active against Vibrio cholera and V. cholera phage.

On the basis of the data presented here, we have assigned the unusual benzofulvene structure (I) to frustulosin: $H_{C} = 0.$

I OH

Frustulosin, mp 139-140°, $C_{12}H_{10}O_3$ (elemental analysis), MV 202 (ms), had λ_{max} 402, 293, 273 (sh), 249, 237 (sh) (ϵ 6800, 6800, 6700, 19400, 15000), V_{max} 3279, 1645, 1613, and 1522 cm⁻¹. Its mass spectrum showed peaks at 202 (M+, 100%), 187 (M-15, 20%), 174 (M-28, 20%). Its 100 MHz pur spectrum ² showed a doublet of a doublet at 2.06 (3H, J 1.0 and 1.6 Hz) for the C-2 Me, and two doublets of quartets (1H each) at 5.44 (J 1.6 and 2.0 Hz) and 5.52 (J 1.0 and 2.0 Hz) for the C-3 methylene. On decoupling the methyl, these methylene protons appeared as an AB quartet (J 2 Hz, geminal coupling). The C-4 OH appeared as a broad peak around 4.5. The aromatic protons on C-5 and C-6 appeared as an AB quartet (J 9 Hz) at 7.16 and 6.88, respectively. The doublet at 6.88 is further split by the aldehyde proton (J 0.4 Hz). A doublet at 10.31 (1H, J 0.4 Hz) and a singlet at 11.22 (1H) are assigned to the aldehyde and chelated hydroxyl, respectively.

Frustulosin formed a discetate when treated with Ac₂O-pyridine. This had mp 87-88° (pet. ether), $\lambda_{\rm max}$ 330, 285, 275 (sh), 270 (sh), 247 (sh), 239 (ϵ 5900, 9600, 11000, 11000, 21000 and 2200Q), $V_{\rm max}$ 1770, 1709, 1595 and 1170 cm⁻¹. Its 60 MHz pur spectrum showed signals at 2.01 (3H) for the methyl, 2.37 (6H) for the two acetates, 5.43 (1H) and 5.51 (1H) for the methylene protons, 7.07 (1H) and 7.36 (1H) for the aromatic protons, and 10.5 (1H) for the aldehyde). The coupling pattern, A₂XY for the methyl and methylene, and AEX for the aromatic and aldehyde protons was the same as that of the parent compound.

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The ¹³C mar spectrum of I showed an sp² carbon at 23.2 (C-2 Me). All the other carbons were sp². There were signals for five fully substituted carbons at 103.9 (C-2), 110.3 (C-9) 117.9 (C-8), 119.3 (C-7) and 125.5 (C-3), two aromatic CH at 124.3 and 124.4 (C-5 and C-6), two CH-bearing carbons at 150.2 and 156.6 (C-4 and C-1) and a carbonyl at 195.8 (CHO). A signal at 119.6 was assigned to the exocyclic methylene.

The evidence presented here is compatible only with structure I. This structure may be looked at as an enolyzed form of a 2,3-dimethyl-1-indenone, stabilized by hydrogen bonding with the aldehyde carbonyl.

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Footnotes and References:

- This culture was received from Dr. Ross W. Davidson (No. 24059), U.S.D.A., December 1943.
 Frustulosin was isolated in crystalline form and tested for biological activity in 1954.
- The nmr spectra were taken in CDCl_s solution with TMS as an internal standard, and are expressed in ppm values on the 8 scale.
- Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, 2nd edition,
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