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THE STEREOCHEMISTRY OF POLYPORENIC ACID A METHYL ESTER

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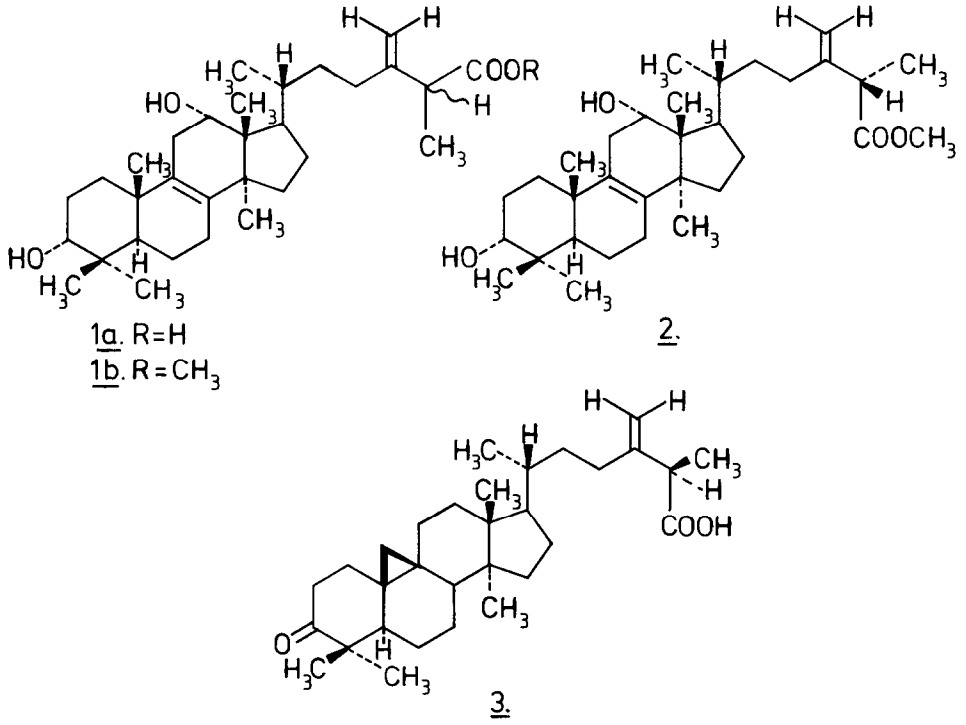
Summary: The absolute configuration of the terminal asymmetric carbon centre in the side-chain of the methyl ester of polyporenic acid A, from Piptoporus betulinus Fries, is shown to be 25(S)(2).

The Basidiomycetous fungus, Piptoporus betulinus Fries contains four structurally related tetracyclic triterpenoid acids,[1] the most abundant of which is polyporenic acid A. The gross structure of this acid (1a) was originally assigned on the basis of degradation studies,[2,3,4] but the stereochemistry of the asymmetric C-25 atom was not investigated. Furthermore, investigations into the side-chain alkylation mechanisms operating in fungi have been in progress for a considerable period of time.[5,6,7] Thus, if both the absolute configuration of the C-25 asymmetric centre and the biosynthetic origin of the carboxyl carbon atom in polyporenic acid A are known, then it is possible to infer the stereochemistry of the introduction of the methyl group which becomes the C-24 exocyclic methylene group in that molecule. In view of this it was decided to establish the absolute configuration of the terminal asymmetric carbon atom in the acid by a single crystal X-ray crystallographic analysis of the easily crystallised methyl ester (1b).

Methyl polyporenate A was crystallised three times, as needles, from aqueous methanol (melting point 148.5 - 149.5°C, lit.m.p.[2] 148.5 - 149.5°C). Spectroscopic analyses were consistent with the molecular structure obtained from the crystallographic analysis. A single crystal of methyl polyporenate A was mounted on an Enraf Nonius CAD4 diffractometer. Accurate lattice parameters were obtained by least squares refinement of the positions of 25 reflections with θ approximately 30°. Intensity data were collected with CuK_α radiation and a variable speed, 1.1°, ω/θ scan technique for $\theta \leq 66°$. Of the 2914 reflections surveyed in this fashion 1662 were judged observed ($|F_o| \geq 2\sigma(F_o)$) after correction for Lorentz, polarisation and background effects,

† The late Professor T.J. King.



but adsorption corrections were not applied. Data reduction and subsequent crystallographic calculations were performed using the CRYSTALS system of programs.[8]

Crystal data:- $C_{32}H_{52}O_4$, M = 500.8 Orthorhombic, a = 11.506(1), b = 13.723(1), c = 18.734(2) Å, U = 2958.05 Å^3, z = 4, D_c = 1.12 g cm^{-3}, space group $P2_12_12_1$ uniquely from systematic absences. CuK_α radiation λ = 1.54178 Å. $\mu(CuK_\alpha)$ = 5.67 cm^{-1}.

The structure was solved by direct methods using the MULTAN[9] program. The resulting E map revealed 34 of the 36 non-hydrogen atoms in the molecule. The remaining 2 atoms were readily located in a ΔF synthesis. Full-matrix least squares refinement with anisotropic carbons and oxygens was carried out to convergence. A difference synthesis revealed the approximate positions of most of the hydrogen atoms. Accurate positions for the hydrogen atoms bonded to carbon were then calculated from geometric considerations. The positions of hydroxyl hydrogen atoms were taken from peaks in the difference map. The hydrogen atoms were then included in the structure factor calculations with isotropic vibrations but without refinement. Final convergence was reached with the crystallographic residual R of 0.0461 and R_w 0.054. A computer generated perspective drawing of the final X-ray model is shown in figure 1.[10,12] The absolute configuration shown is assumed. The molecules are held in the crystal structure by a framework of inter molecular hydrogen bonds from the

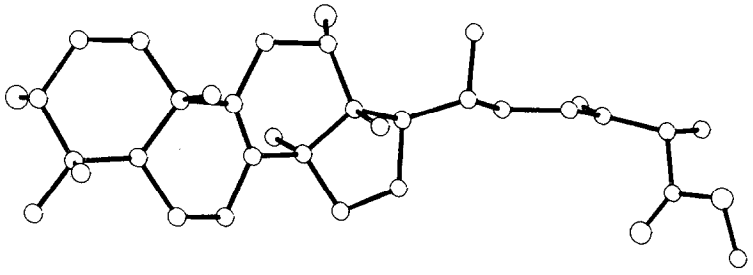


Figure 1

Computer-generated perspective drawing of (25S)-methyl polyporenate A.

hydroxyl groups. Hydrogen bonds of 2.92 Å were found from O(1) to O(2) at ($1\frac{1}{2}$-x, -y, $\frac{1}{2}$ + z) and 2.91 Å from O(2) to O(3) at (1-x, y-$\frac{1}{2}$, $\frac{1}{2}$-z). Bond distances and angles agree well with generally accepted values.

This X-ray diffraction analysis not only supplies the absolute configuration of the C-25 centre, it also confirms in totality the structure originally assigned to polyporenic acid A by degradation studies. The information concerning the absolute configuration of C-25 in polyporenic acid A was used in combination with the results from biosynthetic investigations with P.betulinus Fries (to be published elsewhere) to specify the stereochemistry of the alkylation mechanism operating in the fungus. Finally, it is also of interest to note that the 25 (S) stereochemistry of polyporenic acid A is opposite to the 25 (R) stereochemistry of ambonic acid (3) from the higher plant Mangifera indica.[11] This difference in stereochemisty maybe of phylogenetic significance.

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10. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW. Any request should be accompanied by the full literature citation for the communication.

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12. Structure factor data are available. See Announcement to Authors, Tetrahedron Letters, 47, 5184 (1983).

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