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FOMAJORIN S AND D FROM *FOMES ANNOSUS* (FR) COOKE

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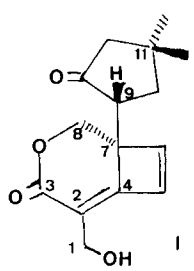
Abstract: Fomajorin S and D, two new isocoumarins have been isolated from the sporophores and ageing cultures of *Fomes annosus*, and have been assigned structures 2 and 3 respectively on the basis of spectroscopic evidence of the natural products and their derivatives.

Fomes annosus (Fr) Cooke (syn. *Heterobasidion annosum* (Fr) Bref), one of the few wood-destroying Basidiomycetes which causes death of the host cell, produces a diverse range of metabolites: fomannosin 1[1], fomannoxin[2a], 7α,8β,11-drimantriol[2b], and 6-methyldehydro-α-lapechone[2c]. In the course of continuing studies on the fungus, we have isolated from sporophores and from ageing cultures two new metabolites for which the names fomajorin S 2 and fomajorin D 3 are proposed[3] (fomannosin numbering). We herein report on the structural elucidation of these metabolites.



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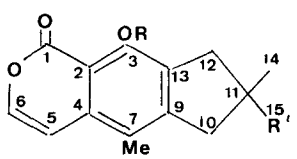
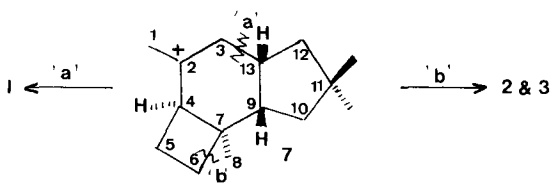


2 R = H; R' = COOH
3 R = H; R' = Me
4 R = H; R' = CO_2Me
5 R = Ac; R' = CO_2Me
6 R = H; R' = CH_2OH



The molecular formula $C_{15}H_{14}O_5$ of fomajorin S 2 (m.p. 243-245°C; $[\alpha]_D^{21°}$ -12.61° (c, 0.16, Me_2CO)) was established by elemental analysis and by mass spectrometry. The ir spectrum (KBr) showed two carbonyl bands at 1708 (carboxyl) and 1688cm^{-1} (chelated δ-lactone) and hydroxyl bands at 3200cm^{-1}. Esterification of 2 gave a crystalline methyl ester 4 (m.p. 187°C; $[\alpha]_D^{21°}$ -21.3° (c, 0.012 $CHCl_3$)) with a molecular formula $C_{16}H_{16}O_5$ established by high resolution mass spectrometry (M^+ 288.1003). The phenolic nature of the chelated hydroxyl group is revealed by a colouration with ferric chloride and acetylation to afford 5 (m.p. 144-145°C; $[\alpha]_D^{21°}$ -22.18 (c, 0.013, $CHCl_3$); ν_{CO}($CHCl_3$) 1770, 1731 and 1720cm^{-1}; δ_H 2.41 (OAc))[4]. The 250 MHz ^1H nmr spectrum of 4, displayed signals due to a tertiary methyl group and an aromatic methyl group (δ_H 1.4 and δ_H 2.25, respectively).

Double resonance experiments identified the two isolated methylene groups as double doublets (δ_H 2.90, 3.47, dd, J 17.0 Hz and δ_H 2.96, 3.54, dd, J 16.9 Hz) and the system O-CH=CH-Ar (δ_H 6.63, 7.20, dd, J 5.9 Hz). The signals for this double bond in the monoacetate 5 disappeared on catalytic hydrogenation with concomitant appearance of two triplets at δ_H 3.01 and δ_H 4.53 (J 6.0 Hz). The ^{13}C nmr spectrum of the ester 4 showed the presence of the following: $3CH_3$, $2CH_2$, a quaternary C, 2CH=, $6sp^2$ fully substituted carbons and two CO signals (δ_C 166.79 and 177.47) and accounted for 15 protons, the remaining proton was observed as D_2O exchangeable in the ^1H nmr spectrum[4]. Reduction of the methyl ester 4 with $NaBH_4$ afforded the carbinol 6 (m.p. 155-156°C, ν(KBr) 3600, 1684cm^{-1}). The observed upfield shift of the aliphatic methyl (δ_H 1.56) in the ^1H nmr spectrum confirmed its general relationship to the primary alcohol; these data are consistent with structure 2 for fomajorin S and structures 4 - 6 for its derivatives. A paucity of material and the unsuitability of crystalline derivatives for X-ray analysis prevented the assignment of the configuration of C-11.

Fomajorin D 3 (m.p. 126-127°C; ν(KBr) 3240, 1675cm^{-1}) is optically inactive and has a molecular formula $C_{15}H_{16}O_3$ (M^+ 244.1099). It differs from fomajorin S 2 in possessing a methyl group in place of the COOH function at C-11 as clearly evidenced by its spectroscopic data. The ^1H nmr spectrum of 3, similar to that of 2, displayed signals due to two aliphatic methyl groups (δ_H 1.19), an aromatic methyl group (δ_H 2.23) and singlets for the two isolated methylene groups (δ_H 2.7 and 2.73) in addition to the signals δ_H 6.63, 7.18, J 6.0 Hz for the system OCH=CHAr. The ^{13}C nmr spectrum resembles that of fomajorin S 2 and fully supports the assigned structure 3.

Biosynthetic studies indicate that the fomajorin D 3 and hence fomajorin S 2 arise from mevalonate via a protoilludyl cation 7 or its equivalent[5]. The isocoumarins isolated previously from fungi have a mono or a disubstituted double bond and were proved to arise biosynthetically from polyketide[6].

Recently, the production of crystals was observed on hyphae during in vitro investigations of antagonistic interrelationships between *Fomes annosus* and other fungi[7]. The unknown compound, which was called liobin ($C_{15}H_{16}O_3$) is apparently fomajorin D 3.

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3. Presented at the IUPAC 12th International Symposium on the Chemistry of Natural Products in Tenerife, 1980.

4. Satisfactory elemental analysis, ir, uv, ^1H nmr, and ^{13}C nmr for fomajorins S and D and their derivatives.

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