The hydroxylation of some longifolanes by *Mucor plumbeus*

Simone Fontes Arantes, James R. Hanson* and Peter B. Hitchcock

Department of Chemistry, University of Sussex, Brighton, Sussex BN1 9QJ, UK

J. Chem. Research (S), 2003, 531–532
J. Chem. Research (M), 2003, 0959–0971

The microbiological hydroxylation of 15-hydroxylongifolane and 15-hydroxyisolongifolane by *Mucor plumbeus* afforded the 10β-hydroxy derivatives whilst 10-oxolongifolane gave the 3α- and 4α- hydroxylated products. The structures of the metabolites were established by X-ray crystallography.

Keywords: microbiological hydroxylation, longifolanes, sesquiterpenoids, *Mucor plumbeus*

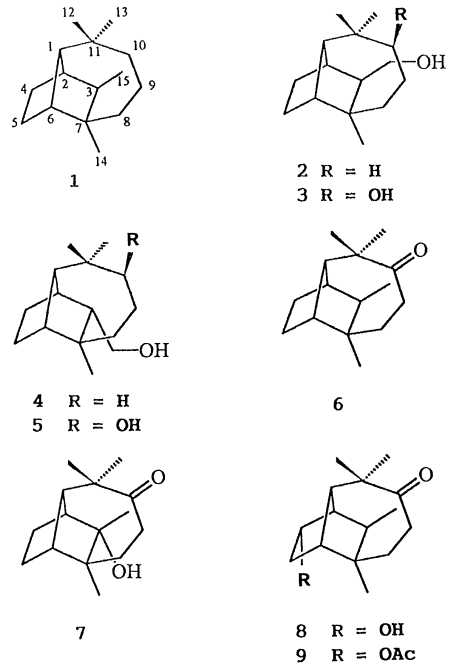
The sesquiterpenoid longifolane skeleton contains a rigid camphane system bridged by a four-carbon chain.[1] This polycyclic carbon skeleton makes this group of sesquiterpenoids suitable substrates for mapping the three-dimensional shape of microbial hydroxylases and in particular the stereochemical relationships that might exist between a binding group and the site of hydroxylation.[3]

Longifolane **1** was converted by hydroboration and oxidation of the borane with alkaline hydrogen peroxide to 15-hydroxylongifolane **2** and a mixture of the 10α- and 10β-hydroxylongifolanes.[4] Oxidation of the latter with chromium trioxide gave the 10-ketone **6**.[4] 15-Hydroxyisolongifolane **4**[5] was available commercially. The compounds **2**, **4** and **6** were used as substrates for hydroxylation by *Mucor plumbeus*.

Incubation of 15-hydroxylongifolane **2** with *M. plumbeus* for five days afforded one major metabolite, 10β, 15-dihydroxylongifolane **3** the structure of which was established by X-ray crystallography (see Fig. 1).

Incubation of 15-hydroxyisolongifolane **4** with *M. plumbeus* also gave a 10β, 15-hydroxyisolongifolane **5**. The location of the additional secondary alcohol (δ_H 3.89; δ_C 74.7) at C-10 followed from significant downfield shifts to the resonances assigned to C-9 (Δδ 15.5ppm) and C-11 (Δδ 4.9ppm). The stereochemistry was assigned by comparison of the ^{1}H NMR spectrum with that of **3** and on the basis of a nuclear Overhauser effect enhancement of the signal at δ_H 3.89 on irradiation of the H-13 signal.

Incubation of 10-oxolongifolane **6** with *M. plumbeus* gave three metabolites which were separated by chromatography. The structure of the major metabolite **7** was established by X-ray crystallography (see Fig. 2). The ^{1}H and ^{13}C NMR spectra of the minor metabolites, **8** and **9** suggested that they were related as an alcohol and its acetate ester. The structure of the alcohol **8** was established by X-ray crystallography (see Fig. 3).



As with other microbiological hydroxylations, these transformations introduced functionality at chemically inaccessible sites in the molecule. However, more interestingly it is possible to superimpose the oxygen functions that were originally present in each of the substrates and rotate the structures so that the hydroxyl groups that are introduced become almost co-incident. In each case the bulk of the substrate occupies the same volume. This suggests that it may be possible to construct a three-dimensional predictive model for these hydroxylations.

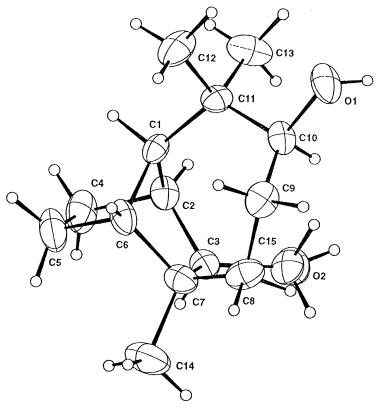


Fig. 1 X-ray crystal structure of compound **3**.

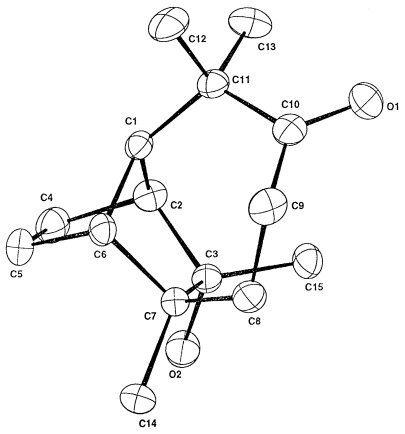


Fig. 2 X-ray crystal structure of compound **7**.

* To receive any correspondence.

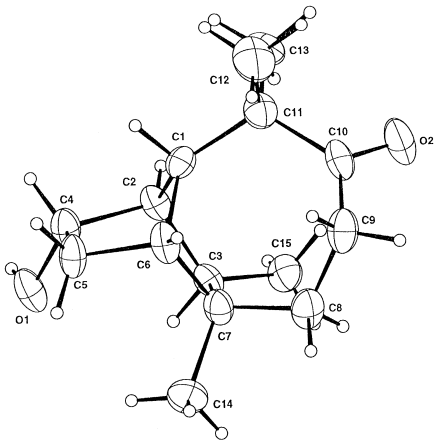


Fig. 3 X-ray crystal structure of compound **8**.

S. F. A. thanks CNPq (Brazil) for financial assistance.

Techniques used: ^{1}H and ^{13}C NMR, X-ray crystallography, IR, MS, microbiological transformation

Table: 1 ^{13}CNMR data

References 5

Received 24 May 2003; accepted 4 July 2003
Paper 03/1621

References cited in this synopsis

1 S. Dev, *Progress in the Chemistry of Organic Natural Products*, 1981, **40**, 49.
3 S.F. Arantes, J.R. Hanson and P.B. Hitchcock, *J. Chem. Research (S)*, 1999, 314-315; (*M*) 1415-1438.
4 J. Lhomme and G. Ourisson, *Tetrahedron*, 1968, **24**, 3167
5 S.G. Patnekar and S.C. Bhattachartyya, *Tetrahedron*, 1967, **23**, 919.