Phytuberin; Revised Structure from the X-Ray Crystal Analysis of Dihydrophytuberin

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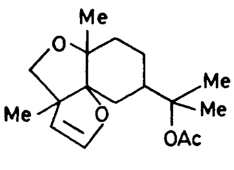
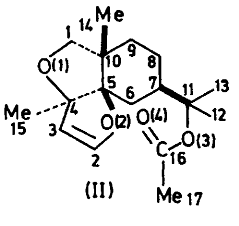
Summary A revised structure for phytuberin is established from the crystal structure of dihydrophytuberin.

Potato tubers inoculated with the late blight fungus *Phytophthora infestans*[1] or the bacterium *Erwinia carotovora* var *atroseptica*[2] accumulate the stress metabolite phytuberin, a liquid antifungal sesquiterpenoid. Possible structures for phytuberin have been proposed by Varns, Kuć,[3] and Coxon *et al.*[4] Several alternative structures appeared to be consistent with the detailed spectral and chemical data obtained on phytuberin and its derivatives.[4] Compound (I) was finally chosen since its carbon skeleton was the only one containing three intact isoprene units although linked in a somewhat unusual manner as a menthane monoterpene skeleton with a C_5 side chain.

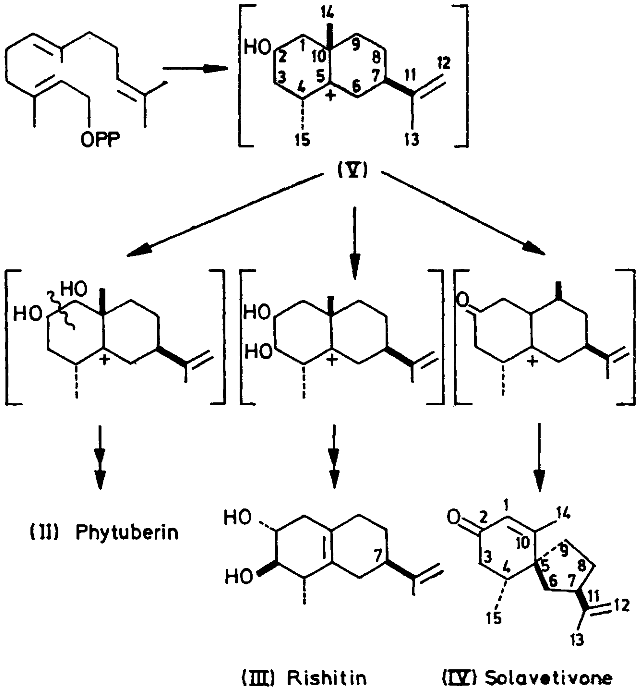


(I)



(II)

Crystalline dihydrophytuberin, $C_{17}H_{28}O_4$, m.p. 66°, was prepared by catalytic hydrogenation of phytuberin and the crystal structure of this product is now reported; the



correct structure for the parent compound, phytuberin, could then be determined.

Dihydrophytuberin crystals are monoclinic, space group $P2_1$, $a = 9{\cdot}723$, $b = 10{\cdot}722$, $c = 8{\cdot}107$ Å, $\beta = 101{\cdot}29°$, $Z = 2$. Intensity data were collected on a Nonius CAD-4 automated diffractometer with monochromated Cu-K_α radiation.

A fragment of the structure was found by direct methods using the program MULTAN,[5] and the remaining carbon and oxygen atoms were located in an electron-density map. Refinement was rapid, and all the hydrogen atoms were located in a difference map. At present, $R = 0{\cdot}091$ for 1650 reflections measured, *i.e.* data for $2\theta \leqslant 140°$.

It is known[4] that the C=C double bond in the parent compound, phytuberin, must be between C(2) and C(3), and the structure of phytuberin is thus established as (II) or the inverse of (II); it is not possible at this stage to distinguish by crystallographic methods the natural enantiomer of phytuberin.

Bond lengths and angles involving the carbon and oxygen atoms all appear normal, within their standard deviations of 0·010 Å and 0·6°.

The six-membered ring has a chair conformation; the substituent bonds C(5)–O(2), C(7)–C(11), and C(10)–C(1) are equatorially arranged. The five-membered ring containing O(1) has an envelope shape, with C(10) lying 0·51 Å out the mean place of the other four atoms. In the other five-membered ring, the conformational strain is more apparent, and C(2) and C(3) are displaced 0·22 and 0·38 Å on opposite sides of the plane through the other three atoms.

The molecule is compact; the acetate group folds round, so that O(4) is 3·02 Å from C(7), 3·01 Å from C(12) and 3·52 Å from C(15). Other short intramolecular distances include C(1) . . . C(2) 3·19 Å, C(7) . . . C(15) 3·31 Å, and C(14) . . . O(2) 2·79 Å. Contacts with neighbouring molecules are by van der Waals forces.

This revised structure allows us to postulate a possible biogenetic relationship between phytuberin (II) and other stress metabolites of potato such as rishitin (III) and solavetivone (IV)[6] through a common hypothetical eudesmane-related intermediate (V) (Scheme). The absolute configuration of phytuberin may thence be predicted as (II), since the conformation at C(7) of rishitin is known.[7]

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