

Cyclodehydroisolubimin: a New Tricyclic Sesquiterpene from Potato Tubers Inoculated with *Phytophthora infestans*

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Summary Cyclodehydroisolubimin (**1**), a new tricyclic sesquiterpene has been isolated from potato tubers inoculated with *Phytophthora infestans*; its structure was derived largely from proton and carbon n.m.r. spectra and its structure and relative stereochemistry confirmed by direct comparison with the ketone derived from a known synthetic intermediate (**2**).

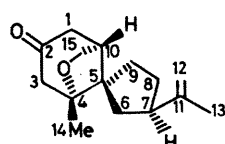
POTATO tubers inoculated with fungi produce a number of sesquiterpene stress compounds with structures based on a vetispirane skeleton,¹ including (–)-solavetivone (**3**)² and isolubimin (**4**).³ We report here the isolation and structure of a new tricyclic sesquiterpene ketone (**1**) which is closely related.

Cyclodehydroisolubimin (**1**) was isolated as a minor component from a chloroform extract of freeze-dried tissue from potato tubers (cv. Pentland Dell) inoculated with a complex race of the blight fungus (*P. infestans* race 1.2.3.4)

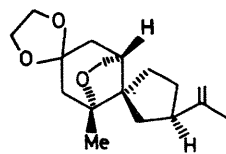
which had earlier furnished (**3**) as a major component. The extract, equivalent to 14 kg of fresh potato tissue, after sequential column chromatography on neutral alumina and silica gel provided a fraction which when purified by preparative gas chromatography gave 10 mg of (**1**) as a mobile oil: $[\alpha]_D^{26} - 6.5^\circ$ (c 0.46, CHCl₃); *m/e* 234 (*M*⁺, C₁₅H₂₂O₂, 32%); ν_{MAX} 1725 (C=O), 3080, 1650, 890 (isopropenyl group), and 1087 cm⁻¹ (cyclic ether); ¹H n.m.r. (CDCl₃): δ 1.22 (3H, s), 1.76 (3H, br s), 2.50 (2H, br s), 3.64 (1H, d, H_B, *J*_{AB} 8.9 Hz), 3.98 (1H, m, H_A, *J*_{AB} 8.9, *J*_{AM} 5.3, and *J*_{AX} 2.3 Hz), and 4.74 (2H, m); ¹³C n.m.r. (CDCl₃): 210.1 (s), 148.2 (s), 108.9 (t), 83.5 (s), 71.7 (t), 54.6 (s), 52.9 (t), 47.0 (d), 46.0 (d), 45.6 (t), 35.2 (t), 32.9 (t), 30.7 (t), 21.4 (q), and 21.2 (q) p.p.m.

These data indicated that (**1**) was tricyclic. Only one olefinic double bond and one carbonyl group (saturated six-membered ring ketone) were present. No hydroxy group was present and the second oxygen atom had therefore to be accommodated in a cyclic ether function. A key feature of the ¹H n.m.r. spectrum of (**1**) was the presence of the two multiplet signals at δ 3.64 and 3.98. The observed splitting pattern for these two signals, which represent a methylene group adjacent to an ether function, required a part structure (**5**) where *J*_{BM} = *J*_{BX} = ca. 0. This requirement is satisfied if the angle H_B-C-C-H_M approaches 90° and *J*_{AX} (2.3 Hz) is a long range coupling as is *J*_{BX} (ca. 0). Spin decoupling experiments established that H_A was coupled to signals centred at δ 2.27 and 2.62. Double irradiation at δ 2.27 removed the 5.3 Hz coupling to H_A whereas irradiation at δ 2.62 removed the 2.3 Hz coupling. Thus, part structure (**5**) was compatible with full structures (**6**) or (**7**) of which (**6**) would be preferred since it is very closely related to other sesquiterpene stress compounds of potato.¹

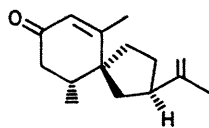
In a recently reported total synthesis of (±)-solavetivone (**3**) by Yamada *et al.*⁴ the two epimeric acetals (**8a**) and (**8b**) were prepared and their stereochemistries confirmed by



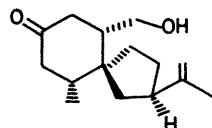
(1)
(±)-(9)



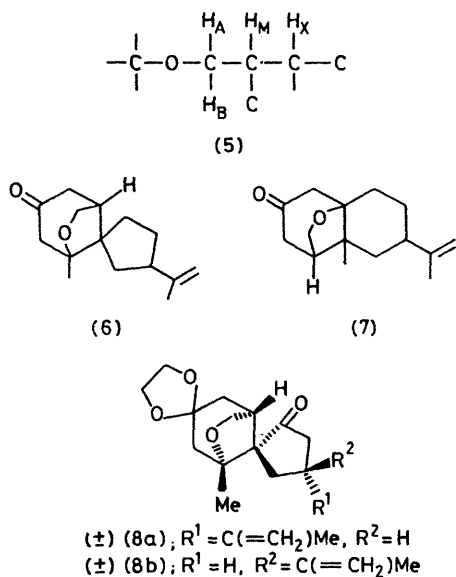
(±)-(2)



(3)



(4)



X-ray crystallography. Wolff-Kishner reduction of (8a) provided in 85% yield the C-7 epimer of (2) which was used for the synthesis of solavetivone. Similarly Wolff-Kishner reduction of (8b) provided the acetal (2) which on hydrolysis [(CO₂H)₂ in aqueous methanol, room temp.] gave the racemic ketone (9).⁵ The ketone (9) prepared from a sample of (8b) was compared chromatographically (g.l.c. and t.l.c.) and spectroscopically (mass spectrometry, ¹H n.m.r., and ¹³C n.m.r.) and found to be indistinguishable from the natural product (1). In particular the remarkable coincidence of the signals in the ¹³C n.m.r. spectra of (1) and (9) (within 0.02 p.p.m. for all except the carbonyl carbon) provided strong evidence for the structural and stereochemical identity of (1) and (9); this finding clearly eliminated (7) and the other three stereoisomers of (1) from consideration.

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