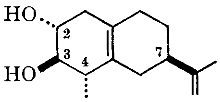
The Structure of Rishitin, a New Antifungal Compound from Diseased Potato Tubers

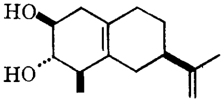
N. KATSUI, A. MURAI, M. TAKASUGI, K. IMAIZUMI, and T. MASAMUNE*
(*Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo, Japan*)

and K. TOMIYAMA
(*Hokkaido National Agricultural Experiment Station, Sapporo, Japan*)

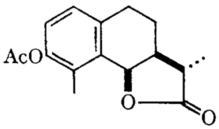
WE recently reported the isolation of a new antifungal compound, designated as rishitin and qualified as "phytoalexin", from tuber tissues of white potatoes (*Solanum tuberlosum* and *S. demissum*) infected by an incompatible race of *Phytophthora infestans*.[1] We present here evidence that the compound is represented by the formula (Ia) or (Ib).



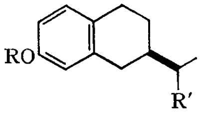
(Ia)



(Ib)



(V)



(IV) R=CO·$C_6H_3(NO_2)_2$, R'=Me
(VI) R=Ac, R'=CO_2H
(VII) R=H, R'=CH_2OH

Rishitin (I), m.p. 65—67°, $[\alpha]^{20}$ −29° (EtOH), was analyzed for $C_{14}H_{22}O_2$ (M^+ 222), and gave the diacetate (Ia), m.p. 70—71°, $[\alpha]_D^{20}$ −6·2°, which was reconverted into (I) by saponification. On hydrogenation over platinum in ethyl acetate, (I) gave its dihydro-derivative (II), $C_{14}H_{24}O_2$ (M^+ 224), m.p. 64—66°, $[\alpha]_D^{20}$ −8·7°, which consumed *ca.* 1·2 mole of perbenzoic acid and showed an intense yellow colour with tetranitromethane, and also gave the diacetate (IIa), m.p. 79—81°, $[\alpha]_D^{20}$ +4·3°. Further hydrogenation of (II) over rhodium–platinum[2] in ethanol produced tetrahydrorishitin (III) (50%), $C_{24}H_{28}O_2$ (M^+ 226), m.p. 112—114°, a negative tetranitromethane test. These chemical and their u.v. (EtOH), i.r., and n.m.r. (CCl_4) spectral data indicate that (I) contains the following structural units: a secondary methyl group [(I) τ 8·88 (3H, d, J = 6 c./sec.); (IIa) 8·98 (3H, d, J = 6·5 c./sec.)]; an isopropenyl group [(I) ν_{max} (film) 1640 and 890 cm.$^{-1}$, τ 8·30 (3H, singlet) and 5·36 (2H, broad); (II) ν_{max} (CCl_4) 1386 and 1370 cm.$^{-1}$, and no absorption near 1640 and 890 cm.$^{-1}$; (IIa) τ 9·10 (6H, d, J = 6 c./sec.)]; a tetra-substituted double bond [(I), (II), and (III) only end-absorptions (log ϵ 3·89, 3·74 and <2·8 at 205 mμ, respectively, *cf.*, cholesterol and 5α-cholesterol, log ϵ 3·58 and 2·82 at 205 mμ); (II) no absorption below τ 5·0]; two secondary hydroxyl groups [(I) ν_{max} (film) 3320 cm.$^{-1}$, τ 6·88 (1H, t, J = 9 c./sec.) and 6·45 (1H, q, $J \simeq 5 \sim 6$ and 9 c./sec.); (Ia) ν_{max} (Nujol) 1745 and 1250 cm.$^{-1}$, τ 8·00, 7·96 (each 3H, s) and 5·20 (2H, br), and no absorption near τ 6·5]. Dehydrogenation of (II) with selenium produced a 60% yield of eudalene; (the picrate, m.p. 92—93°, and the trinitrobenzene adduct, m.p. 113—114°).[3] Rishitin (I) consumed 0·96 mole of periodic acid at room temperature for 20 hr. [*cf.* (Ia) 0·04 mole], and the resulting dialdehyde showed no absorption due to an $\alpha\beta$-unsaturated carbonyl function in the i.r. spectrum, ν_{max} (film) 2700, 1725 (CHO), and 1645, 890 cm.$^{-1}$ ($C{=}CH_2$). Thus, the planar formula (I) is proposed for rishitin.

Oxidation of compound (II) with Jones reagent in a heterogeneous mixture of ether and water[4] followed by acid treatment produced a mixture of phenols, from which a 3,5-dinitrobenzoate (IV), $C_{21}H_{22}O_6N_2$, m.p. 159—160°, $[\alpha]_D^{20}$ +56°, was isolated after treatment with 3,5-dinitrobenzoyl chloride and subsequent purification by preparative t.l.c. On the other hand, a phenol lactone[5] (V), prepared from santonin, was submitted to hydrogenolysis over palladium–charcoal in acetic acid to yield an amorphous phenol acid (VI), which was then reduced with lithium aluminium hydride to an alcohol (VII), m.p. 128—130°. The ditoluene-*p*-sulphonate (VII) formed therefrom, gave on hydride reduction followed by acylation, a 3,5-dinitrobenzoate, m.p. 159—160°, $[\alpha]_D^{20}$ +60°, in an over-all yield of 45% from (V), which was identical with (IV) derived from (II) in all respects. This correlation confirms the structure (I) and also elucidates the absolute configuration of C-7.

The relative configurations of a methyl (C-4) and two hydroxyl groups (C-3 and C-2) in (I) are deducted by comparison of the n.m.r. spectra of (I) and its dihydro-dibromo-derivative (VIII), m.p. 129—130°, τ (C_5D_5N) 5·77 (1H, t, $J = 9$ c./sec., C*H*-OH) and 5·17 (1H, q, $J \simeq 5 \sim 6$ and 9 c./sec.), prepared in a good yield by treatment of (II) with bromine in chloroform. Both the compounds showed almost the same absorption patterns, a triplet and a quartet, due to the protons at C-3 and C-2, indicating that the ring in question of (I) adopts a half-chair conformation and the three substituents are all oriented equatorial. Rishitin is, therefore, best represented by the formula (Ia) or (Ib).

(*Received, November* 16*th*, 1967; *Com.* 1243.)

---

[1] K.Tomiyama, T. Sakuma, N. Ishizaka, N. Sato, N. Katsui, M. Takasugi, and T. Masamune, *Phytopathology*, in the press.

[2] S. Nishimura, *Bull. Chem. Soc. Japan*, 1960, **33**, 566.

[3] R. P. Linstead, K. O. A. Michaelis, and L. S. Thomas, *J. Chem. Soc.*, 1940, 1139.

[4] A. E. Vanstone and J. S. Whitehurst, *J. Chem. Soc.* (*C*), 1966, 1973.

[5] S. M. Sharif, S. Nozoe, K. Tsuda, and N. Ikekawa, *J. Org. Chem.*, 1963, **28**, 793.