Rishitin I. The Isolation and Structure Elucidation[1)]

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A modification of the isolation procedure and the details of the structure elucidation of rishitin (**1**) are described.

One decade ago we reported in preliminary communications[2)] on the isolation and structure of rishitin, an antifungal norsesquiterpene qualified as "phytoalexin",[3)] from tuber tissues of white potatoes (*Solanum tuberlosum*×*S. demissum*) infected by an incompatible race of *Phytophthora infestans*. Since the isolation of rishitin, a number of sesquiterpenes have been isolated and characterized as antifungal stress metabolites from various plants of the Solanaceae in our and other laboratories.[4)] In this paper we describe our recently modified isolation procedure of rishitin from diseased potatoes, leading to separation of thermally unstable compounds, and the details of its structure determination.

Tuber slices of R_1 cultivar "Rishiri" (338 kg) were inoculated with a zoospore suspension of an incompatible race of *Phytophthora infestans* (Mont.) de Bary, race 0, and incubated at 18—20 °C for 2 days. The inoculated slices were stored in an ice-box (−30 °C) for a week, and then immersed in methanol at room temperature for a week. The methanol extracts were concentrated below 30 °C and extracted with chloroform. The chloroform extracts were treated with acetone and then with hexane to remove the respective solvent-insoluble meterials, and the resulting hexane-soluble fraction was evaporated to leave an oily residue (160 g), which was dissolved in ether. The ether solution, after removal of acidic and basic components, gave a neutral syrup (107 g), which contained many compounds as shown in Fig. 1. The neutral syrup was separated over silicic acid and celite, hexane, benzene, ether, acetone, and methanol being used successively as eluents. Fractions eluted with a 1 : 1 mixture of benzene and ether gave crude rishitin (**1**, *ca.* 8.0 g), which was further purified by rechromatography over silica gel to yield rishitin (**1**, 3.9 g), mp 65—67 °C and $[\alpha]_D$ −35.1°,[5)] in pure state.

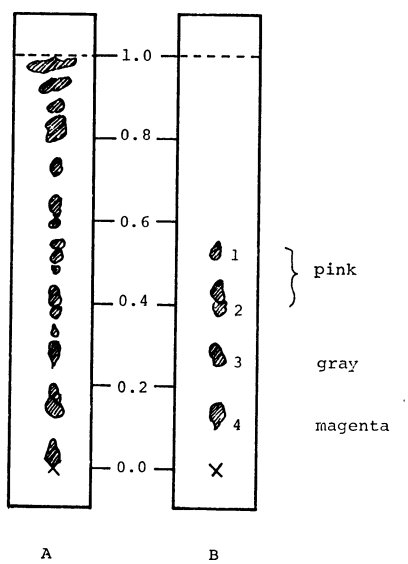
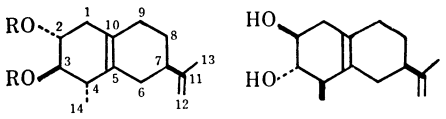


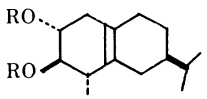
Fig. 1. TLC of the neutral syrup (silica gel, ether).
A, ceric sulfate and B, Ehrlich reagent.
1: Rishitinol, 2: lubimin, 3: rishitin, 4: oxylubimin.



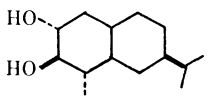
1 R=H **1'**
1a R=Ac
1b R=$COC_6H_3(NO_2)_2$

Rishitin (**1**) was analyzed for $C_{14}H_{22}O_2$ [*m/e* 222 (M^+)] and gave the diacetate (**1a**), mp 70—71 °C and $[\alpha]_D$ −14.1°,[5)] and also the bis(3,5-dinitrobenzoate) (**1b**), mp 172—173 °C and $[\alpha]_D$ −45°, which were reconverted into the starting alcohol (**1**) by saponification. When hydrogenated over platinum in ethyl acetate, compound **1** formed the dihydro derivative (**2**), $C_{14}H_{24}O_2$ [*m/e* 224 (M^+)], mp 64—66 °C and $[\alpha]_D$ −8.7°, which consumed *ca.* 1.2 mol of peroxybenzoic acid and showed an intense yellow color with tetranitromethane, and also gave the diacetate (**2a**), mp 79—81 °C and $[\alpha]_D$ +4.3°. Further hydrogenation of **2** over rhodium–platinum[6)] in ethanol produced tetrahydrorishitin (**3**), $C_{14}H_{26}O_2$ [*m/e* 226 (M^+)], mp 112—114 °C, which was negative to the tetranitromethane test. On the other hand, rishitin consumed 0.96 mol of periodic acid at room temperature for 20 h, and also was converted readily into the acetonide (**4**), mp 32—35 °C, when treated with acetone over silica gel (Wakogel Q-23). These chemical reactions and the UV, IR, and NMR spectral data of each compound indicated that rishitin contains the following structural units: a secondary methyl group [**1**, δ 1.12 (3H, d, J=6 Hz); **1a**, δ 1.06 (3H, d, J=6.5 Hz)]: an isopropenyl group [**1**, ν_{max} 3060, 1640 and 890 cm^{-1}, δ 1.70 (3H, s) and 4.64 (2H, br); **2**, ν_{max} 1386 and 1370 cm^{-1}, and no absorption near 1640 and 890 cm^{-1}; **2a**, δ 0.91 (6H, d, J= 6 Hz)]: a tetrasubstituted double bond [**1**, **2**, and **3**, only end absorptions (log ε 3.89, 3.74, and less than 2.8 at 205 nm, respectively, *cf.*, cholesterol and 5α-cholestanol, log ε 3.58 and 2.82 at 205 nm); **2**, no absorption below δ 5.0]: two vicinal secondary hydroxyl groups [**1**, ν_{max} 3320 cm^{-1}, δ 3.12 (1H, t, J=9 Hz), 3.55 (1H, br do d, J=9 and 7 Hz), and 4.18 (2H, br s, 2OH); **1a**, ν_{max} 1745 and 1250 cm,$^{-1}$

δ 2.00 and 2.04 (each 3H, s), 4.80 (2H, br), and no absorption near δ 3.5; **4**, ν_{max} 1378 and 1370 cm^{-1}; δ 3.18 (1H, t, J=9 Hz) and 3.59 (1H, do t, J=9, 9, and 7 Hz)].



2 R=H
2a R=Ac



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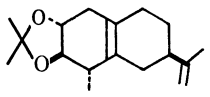

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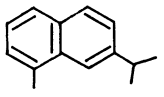
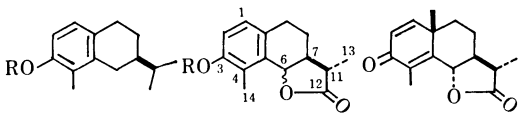


5

Dehydrogenation of dihydrorishitin (**2**) with selenium proceeded smoothly to give eudalene (**5**) in a high (60%) yield, which formed the picrate, mp 92—93 °C, and the trinitrobenzene adduct, mp 113—114 °C.[7] This result, combined with the presence of the functional groups described above, led to proposal of the (planar) formula (**1**) for rishitin. The structure was supported by the ^{13}C NMR spectra of **1**, obtained with proton noise decoupling and also under off-resonance decoupled conditions; manely, the spectra indicated, together with chemical shift considerations,[8] that the skeleton of rishitin consisted of the following carbon units; three C(C=C)–C (δ 148.9, 129.0, and 124.9 for C_{11}, C_5, and C_{10}), one CH_2(=C)–C (109.0 for C_{12}), two C–CH(OH)–C (79.2 and 71.5 for C_3 and C_2), two C–CH(C)–C (41.6 and 40.4 for C_7 and C_4), four C–CH_2–C (38.3, 31.1, 29.7, and 26.5 for C_8, C_6, C_9, and C_1), and two CH_3–C (21.0 and 16.4 for C_{13} and C_{14}).[9]

Oxidation of dihydrorishitin (**2**) with the Jones reagent in a heterogeneous mixture of ether and water[10] followed by acid treatment produced a mixture of phenols, from which a 3,5-dinitrobenzoate (**6a**), $C_{21}H_{22}O_6N_2$ [*m/e* 398 (M^+)], mp 159—160 °C and $[\alpha]_D$ +56°, was isolated in a low (3%) yield after treatment with 3,5-dinitrobenzoyl chloride and subsequent purification by preparative TLC. On the other hand, "6-epi-1-desmethyldesmotroposantonin 3-acetate" (**7b**), prepared from (−)-α-santonin (**8**) *via* a known two-step process,[11] was submitted to hydrogenolysis over palladium–charcoal in acetic acid to yield a phenol acetate acid (**9**), oil, which was converted with diazomethane into the methyl ester (**9a**), oil, and then reduced with lithium aluminium hydride to give a phenol alcohol (**10**), mp 126—127 °C and $[\alpha]_D$ +76.7 °C, in an 86% yield from **7b**. The bis(*p*-toluenesulfonate) (**10a**), oil, obtained from **10**, gave on the hydride reduction a phenol (**6**), oil and $[\alpha]_D$ +85.7°, in a 65% yield from **10**. This phenol (**6**) was converted into its 3,5-dinitrobenzoate, mp 159.5—160 °C and $[\alpha]_D$ +60.1°, which was identical with the dinitrobenzoate (**6a**), derived from **2**, in all respects. This correlation confirms the structure **1** for rishitin and also elucidates the absolute configuration at C_7.

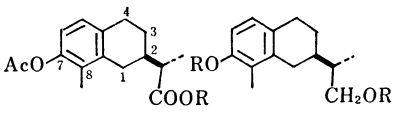
The configurations of a methyl at C_4 and two hydroxyl groups at C_2 and C_3 in rishitin (**1**) were deduced



6 R=H
6a R=$COC_6H_3(NO_2)_2$

7 6β-H, R=H
7b 6α-H, R=Ac

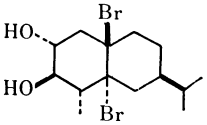
8



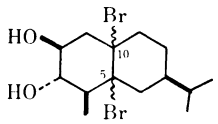
9 R=H
9a R=CH_3

10 R=H
10a R=Ts

from the spectra of **1** and its dihydro-dibromo derivative (**11**), mp 129—130 °C, prepared in good yields by treatment of dihydrorishitin (**2**) with bromine or pyridinium bromide perbromide[12] in chloroform; δ 3.78 (1H, t, J=9 Hz, H at C_3) and 4.32 (1H, do t, J=9, 9, and 7 Hz, H at C_2) for **11**. Both the compounds (**1** and **11**) exhibited almost the same absorption patterns due to the protons at C_3 and C_2, indicating that the ring of **1** in question adopts a half-chair conformation and the three substituents are oriented equatorial, equatorial, and quasi-equatorial at C_2, C_3, and C_4, respectively. Rishitin is, therefore, represented either by the formula **1** or **1′**. Of these formulas, the former structure (**1**) seems to be more favorable on the basis of the following considerations. If rishitin is formulated as structure **1′** the bromination would possibly result in formation of two dibromides (**11′** and **11″**) with comparable instability due to severe 1,3-diaxial interaction(s), assuming the reaction in question proceeded in a kinetically controlled and *trans*-addition manner as observed usually. The situation becomes completely different with formula **1**, and the bromination is expected to produce only one dibromo compound (**11**) of two possible dibromides derivable from **2**. The observed fact that the relevant dibromodihydrorishitin was obtained stereoselectively in a high yield and was recovered unchanged on standing in a refrigerator for 6 months or after repeated recrystallizations, is in line with this expectation. Confirmatory evidence for structure **1** was later presented independently on the basis of the CD spectrum of a chelate complex of rishitin in a cuprammonium solution by Bukhari and Guthrie[13] as well as the CD spectrum of rishitin dibenzoate (the dibenzoate chirality rule) by Harada and Nakanishi.[14] Hence, rishitin is represented correctly by the formula **1**, which has completely been demonstrated by the synthesis (the succeeding paper).[15]



11



11′ 5β-Br, 10α-Br
11″ 5α-Br, 10β-Br

Experimental

All the melting points were uncorrected. The homogenity of each compound was always checked by TLC on silica gel (Wakogel B-5) with various solvent systems, and the spots were developed with ceric sulfate in dil sulfuric acid and/or iodine. The optical rotations, UV and IR spectra were measured in ethanol, ethanol and Nujol, respectively, unless otherwise stated. The NMR and ^{13}C NMR spectra were obtained in chloroform-*d* at 60 and/or 100 MHz, and the chemical shifts were given in δ-values, TMS being used as an internal reference. The abbreviations "s, d, t, m, br, and do" in the NMR spectra denote "singlet, doublet, triplet, multiplet, broad, and double", respectively.

*Isolation of Rishitin (**1**).* *(i) Materials.* Tubers of potato variety, Rishiri *(Solanum tuberosum × S. demissum)*, having the R_1 gene, were used for the experiments. Zoosporangia of an incompatible race of *Phytophthora infestans* (Mont.) de Bary, race 0, were obtained from mycerial mats growing on the cut surfaces of fresh potato tuber slices, Irish Cobbler, having no resistance gene. Zoospores were liberated by holding the sporangial suspensions at 11—12 °C for 2—3 h. Both sides of the tuber slices (338 kg) of 1.5—2.0 mm thickness were inoculated with the zoospore suspension (250000—500000 zoospores/ml), and the inoculated slices were incubated at 18—20 °C for 2 d. Tubers showing abundant brown spots were then stored at −30 °C for a week.

(ii) Extraction and Isolation. The frozen tuber slices were immersed in methanol (250 l) for a week, and the supernatant was separated by decantation. The tubers were re-extracted twice with methanol (2 × 150 l), and the methanol extracts were combined and concentrated to *ca.* 200 l by a film evaporator under reduced pressure (30—60 Torr) below 30 °C. The concentrate was extracted with an equal volume of chloroform under shaking, and the emulsion forming unavoidably was centrifuged to be separated into chloform and aqueous layers. The chloroform layer was evaporated to leave an oily residue. When the residue was treated with acetone (1.2 l), precipitates separated out and were removed by filtration. The filtrate was concentrated again to give an oily residue, which was treated with hexane (1.2 l). After removal of hexane-insoluble materials by decantation and filtration, the hexane solution was evaporated to give oily substances, which were dissolved in ether (5 l) and washed with 10% aq sodium carbonate and then with 0.1 M hydrochloric acid to remove acidic and basic components. The ether solution was washed with water, dried and evaporated to yield a neutral syrup (107 g), which was subjected to chromatographic purification over silicic acid (Mallinckrodt AR-100, 900 g) and celite (300 g), hexane, benzene, ether, acetone and methanol being used as eluents. Eluates with hexane, hexane–benzene (1 : 1) and benzene, on evaporation of the solvents, left oily (Fraction A, 2.1 g), semi-solid (B, 6.2 g), and solid residues(C, 42 g), respectively, the last fraction consisting mainly of higher fatty acids. Fractions D and E (2.5 g and 4.8 g) eluted with benzene–ether (3 : 1) and benzene–ether (3 : 2) contained rishitinol[16] and lubimin,[17] respectively. The following fraction (F), eluted with benzene–ether (1 : 1 and 1 : 2), afforded crude rishitin (8.0 g). Further eluates with benzene–ether (3 : 7) and ether gave an oil (G, 1.7 g) and those with ether–acetone (9 : 1) an oil (H, 2.4 g), the latter containing oxylubimin[17] and lubiminol.[17b] Subsequent fractions eluted with ether–acetone (1 : 1), acetone, acetone–methanol (1 : 1), and methanol were combined to give a resinous oil (I, 3.9 g). The crude rishitin, showing an almost single spot on TLC, was again purified by chromatography over silica gel (Merck 400 g) with ether, each fraction (60 ml) being checked by the NMR spectrum. Fractions (No. 11—40) were combined, crystallized on standing and amounted to 3.9 g.

*Rishitin (**1**), and Its Diacetate, Bis(3,5-dinitrobenzoate), and Acetonide (**1a**, **1b**, and **4**).* *(i)* Rishitin (**1**) had mp 65—67 °C and $[\alpha]_D$ −34.1°,[5] and showed the Mass, UV, IR, NMR, (CCl_4), and ^{13}C NMR spectra, in the text. Found: C, 75.58; H, 9.75%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97%.

A soln of **1** (100 mg) was treated with acetic anhydride (Ac_2O, 0.5 ml) and pyridine (Py, 1 ml) at room temp for 19 h. The reaction mixture was poured into ice-water and extracted with ether. The ether soln was washed with 2 M hydrochloric acid, 5% aq sodium carbonate and water, dried, and evaporated to give **1a** (115 mg), mp 68—70 °C. This was recrystallized from hexane to yield an analytical sample (70 mg), mp 70—71 °C and $[\alpha]_D$ −14.1°;[5] MS, in the text; IR, ν_{max} 1745, 1250, 1645, and 885 cm^{-1}; NMR (CCl_4), δ 1.06 (3H, d, J=6.5 Hz, 14-C$\underline{H}_3$), 1.75, 2.00, and 2.04 (each s, 3H, 13-C$\underline{H}_3$ and 2OCOC$\underline{H}_3$), 4.70 (2H, br s, 12-C$\underline{H}_2$), and 4.80 (2H, br m, 2$\underline{H}$ at C_2 and C_3). Found: C, 70.74; H, 8.51%. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55%.

A soln of crude rishitin (*cf.*, the isolation of rishitin) (279 mg) in benzene (10 ml) and Py (3 ml) was stirred with 3,5-dinitrobenzoyl chloride (760 mg) in benzene (10 ml) at room temp for 15 h, and diluted with ether (30 ml). The soln was washed with 0.5 M hydrochloric acid, water, 1 M aq sodium hydroxide (30 ml) and water, dried and evaporated to leave a crystalline residue (580 mg), which on recrystallization from ethyl acetate gave **1b** (230 mg), mp 172—173 °C and $[\alpha]_D$ −45° ($CHCl_3$). Found: C, 55.14; H, 4.42; N, 9.40%. Calcd for $C_{28}H_{26}O_{12}N_4$: C, 55.08; H, 4.29; N, 9.18%.

(ii) A suspended mixture of **1b** (240 mg) in methanol (20 ml) containing potassium hydroxide (1 M) was refluxed for 1 h under nitrogen. After being cooled, the mixture was mixed with 3 M hydrochloric acid, when the pH value became *ca.* 9.0, and was concentrated and then shaken with water and ether. The ether soln, after being worked up as usual, gave oily rishitin (**1**, 100 mg), showing a single spot on TLC, which was distilled at 90—100 °C (bath temp) under less than 1 mmHg pressure and allowed to stand to give crystalline rishitin (**1**, 83 mg). Compound **1a** was also converted under the same conditions as **1b** to give crystalline rishitin (**1**).

(iii) A suspended mixture of silica gel (Wakogel Q-23, 5 g) in chlorcform was packed in a column, and washed with acetone and then hexane. Compound **1** (10 mg) was passed through the column, using 8% acetone in hexane to yield **4** (10 mg), oil, which was distilled at 100 °C (bath temp) (1 mmHg) to give its crystalline acetonide (**4**, 8.5 mg), mp 32—35 °C; MS, *m/e* 262 (M^+) and 131 (base); IR (liquid), ν_{max} 3080, 1643, 1378, 1370, 1229, 1100, 1083, 1042, and 888 cm^{-1}; NMR (CCl_4), δ 1.13 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 1.39 [6H, s, $(C\underline{H}_3)_2CO$], 1.74 (3H, s, 13-C$\underline{H}_3$), 3.18 (1$\underline{H}$, t, J=9 Hz, $\underline{H}$ at C_3), 3.59 (1H, do t, J=9,9, and 7 Hz, $\underline{H}$ at C_2), 4.59 and 4.68 (each 1H, s, 2$\underline{H}$ at C_{12}). Found: C, 77.70; H, 9.82%. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99%.

Attempted formation of **4** from **1** (14 mg) with *p*-toluenesulfonic acid (7 mg) in dry acetone (5 ml) under reflux or from **1** (10 mg) in acetone (4 ml) containing one drop of 60% aq perchloric acid led to recovery of the starting glycol (**1**). When treated with acetone over anhydrous copper sulfate at room temp for 90 h, compound **1** was converted into **4** only in 20—30% yields.

*11,12-Dihydrorishitin (**2**) and Its Diacetate (**2a**).* A soln of **1** (110 mg) in ethyl acetate (30 ml) was hydrogenated over

Adams platinum (100 mg as $PtO_2 \cdot H_2O$) at room temp for 30 min, when one equiv of hydrogen had been consumed. The reaction mixture was worked up as usual to leave a crystalline substance (118 mg), which was recrystallized from hexane to give **2** (95 mg), mp 64—66 °C and $[\alpha]_D$ −8.7°; MS and UV, in the text; IR (CCl_4), ν_{max} 3360, 1386, and 1370 cm^{-1}. Found: C, 74.52; H, 10.62%. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78%.

Compound **2** (44 mg) was treated with Ac_2O (0.4 ml) and Py (0.8 ml) at room temp for 15 h. The mixture was worked up as usual to give a crystalline substance (60 mg), which was recrystallized from hexane to yield **2a** (38 mg), mp 79—81 °C and $[\alpha]_D$ +4.3°; IR (CCl_4), ν_{max} 1751, 1385, 1369, 1245, 1228, and 1029 cm^{-1}; NMR, δ 0.91 (6H, d, J=6 Hz, 12- and 13-C$\underline{H}_3$), 1.05 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 2.04 and 2.08 (each 3H, s, 2OCOC$\underline{H}_3$), and 4.95 (2H, br m, 2$\underline{H}$ at C_2 and C_3). Found: C, 69.93; H, 8.95%. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15%.

*5,10,11,12-Tetrahydrorishitin (**3**).* A soln of **1** (100 mg) in a 1 : 9 mixture (40 ml) of acetic acid and ethanol was hydrogenated over rhodium-platinum catalyst[6] (60 mg as $Rh_2O_3 \cdot PtO_2 \cdot H_2O$) at room temp for 20 h with shaking. The mixture was worked up as usual to leave an oily residue (100 mg), showing two spots on TLC, which was separated into two fractions by preparative TLC over silica gel. A major, more polar fraction gave a crystalline substance, which on recrystallization from ether afforded **3** (50 mg), mp 112—114 °C; MS and UV, in the text; IR, ν_{max} 3380, 1385, and 1370 cm^{-1}; NMR, δ 0.86 and 0.97 (total 9H, each d, J=6 and 7 Hz, 12-, 13- and 14-C$\underline{H}_3$), and 3.42 (2H, br m, 2$\underline{H}$ at C_2 and C_3).

*5,10-Dibromo-11,12-dihydrorishitin (**11**).* To a soln of **2** (60 mg) in chloroform (1 ml) was added dropwise bromine in chloroform (1.6 ml) (278 mg of Br_2 in 10 ml of $CHCl_3$) with stirring, when crystalline substances precipitated and were collected by filtration and recrystallized from carbon tetrachloride to give **11** (85 mg), mp 129—130 °C. This compound (**11**, 13 mg) was also obtained from **2** (11.2 mg) with pyridinium bromide perbromide[12] (16 mg); $[\alpha]_D$ +30.9°; MS, *m/e* 222 (M^+−2HBr), 204 (M^+−2HBr−H_2O), 186 (M^+−2HBr−$2H_2O$), 161 (204−C_3H_7), and 143 (186−C_3H_7); IR, ν_{max} 3475, 3340 and 1040 cm^{-1}; NMR ($CDCl_3$), δ 0.92 (6H, d, J=6.5 Hz, 12- and 13-C$\underline{H}_3$), 1.22 (3H, d, J=6.5 Hz, 14-C$\underline{H}_3$), 2.44 (2H?, s, 2O$\underline{H}$), 3.78 (1H, t J=9 Hz, $\underline{H}$ at C_3), and 4.32 (1H, do t, J=9, 9, and 7 Hz, $\underline{H}$ at C_2); NMR (C_5D_5N), δ 0.87 (6H, d, J=7 Hz, 12- and 13-C$\underline{H}_3$), 1.54 (3H, d, J=6.5 Hz, 14-C$\underline{H}_3$), 4.31 (1H, t, J=9.5 Hz, $\underline{H}$ at C_3), 4.90 (1H, do t, J=9.5, 9.5, and 6 Hz, $\underline{H}$ at C_2) and 5.93 (2H, s, 2O$\underline{H}$).

*Dehydrogenation of **2** with Selenium.* A mixture of **2** (100 mg) and selenium (170 mg) was heated at 240 °C for 22 h and then at 300 °C for 6 h in a sealed tube, and cooled. The reaction mixture was extracted with ether, and the ether soln was washed with 1 M aq sodium hydroxide and water, dried and evaporated to leave a neutral oil (68 mg), which was distilled at 60—70 °C (bath temp) under reduced pressure (1 Torr) to give an oil (45 mg), showing a single spot on TLC. This was further purified by preparative TLC over silica gel to yield eudalene (**5**, 20 mg) in pure state, which formed the picrate, mp 92—93 °C, and the trinitrobenzene adduct, mp 113—114 °C; (lit,[7] 92.8 °C and 113 °C, respectively).

*Conversion of **2** into (2R)-2-Isopropyl-8-methyl-1,2,3,4-tetrahydronaphthalen-7-ol 3,5-Dinitrobenzoate (**6a**).* To a stirred mixture of **2** (90 mg) in ether (10 ml) and water (5 ml) was added dropwise the Jones reagent[9] (0.5 ml) at room temp,[10] and the whole mixture was further stirred for 1 h. The ether soln was worked up as usual to leave an oily residue (46 mg), which without further purification was refluxed with concd hydrochloric acid (2.5 ml) in methanol (5 ml) for 1 h under nitrogen. The resulting soln was mixed with water (10 ml) and extracted with ether repeatedly. The ether soln, after usual work-up, left an oily residue, showing two mian spots on TLC, which was purified by preparative TLC over silica gel with chloroform. One (less polar) of the two main fractions gave a colorless oil (6 mg), which was treated with 3,5-dinitrobenzoyl chloride (8 mg) in Py (0.5 ml) at room temp overnight and heated on a water bath for 1 h. The soln, after being worked up as usual, gave a crystalline substance, which on recrystallization from ethanol-acetone gave **6a** (3 mg), mp 159—160 °C and $[\alpha]_D$ +56° ($CHCl_3$). Compound **6a** was identical with an authentic sample obtained from (−)-α-santonin in all respects.

*6-Epi-1-desmethyldesmotroposantonin 3-Acetate (**7b**).* This compound (**7b**) was prepared by the procedure of Sharif and coworkers.[11] (−)-α-Santonin (20 g), mp 170—172 °C and $[\alpha]_D$ −172.4°, was stirred with activated zinc powder (200 g) under reflux in *N,N*-dimethylformamide (200 ml) and water (15 ml) for 30 min, and gave 1-desmethyldesmotroposantonin (**7a**, 4.1 g), mp 231—232 °C (acetone) (lit.,[11] 228—229 °C) and $[\alpha]_D$ +105.1° ($CHCl_3$) (lit,[11] +115°); MS, *m/e* 232 (M^+), 217, 204, 189, and 159; IR, ν_{max} 3400, 1764, 1605, 1588, and 812 cm^{-1}; NMR, δ 1.28 (3H, d, J=6.5 Hz, 13-C$\underline{H}_3$), 1.60 (1H, s, O$\underline{H}$), 2.35 (3H, s, 14-C$\underline{H}_3$), 2.93 (2H, br m, W_H=14Hz, 2$\underline{H}$ at C_9), 5.02 (1H, d, J=9 Hz, $\underline{H}$ at C_6), 6.66 and 6.83 (each 1H, ABq, J=8 Hz, 2$\underline{H}$ at C_2 and C_1).

A soln of **7a** (1.76 g) in Ac_2O (28 ml) containing 7 drops of concd sulfuric acid was heated on a water bath for 20 min, and gave **7b** (1.78 g), mp 157.5—158 °C (methanol) (lit,[11] 159.5—160.5 °C) and $[\alpha]_D$ −170.8° ($CHCl_3$) (lit,[11] −155.7°); Mass, *m/e* 274 (M^+), 232 (base, M^+−CH_2CO), 217, 188, 173, and 159; IR, ν_{max} 1769 and 1747 cm^{-1}; NMR, δ 1.40 (3H, d, J=7 Hz, 13-C$\underline{H}_3$), 2.25 and 2.34 (each 3H, s, 14-C$\underline{H}_3$ and OCOC$\underline{H}_3$ or *vice versa*), 5.59 (1H, d, J=5.5 Hz, $\underline{H}$ at C_6), and 6.98 (2H, s, 2$\underline{H}$ at C_1 and C_2). The overall yield amounted to 18.7% (lit,[11] 12.2%).

*2-(7-Acetoxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)propanoic Acid (**9**) and Its Methyl Ester (**9a**).* A solnof **7b** (3.00 g) in acetic acid (50 ml) was hydrogenated over 5% palladium charcoal (Wako, 1.5 g) at room temp for 20 h, when 327 ml (1.24 equiv) of hydrogen had been consumed. The mixture was filtered to remove the catalyst, which was washed with chloroform. The filtrate and washings were combined and evaporated to leave a foamy residue (**9**, 3.33 g), showing a single spot on TLC, after azeotropization; IR ($CHCl_3$), ν_{max} 1750, 1702, 1601, and 1063 cm^{-1}; NMR, δ 1.30 (3H, d, J=6 Hz), 2.01 and 2.32 (each 3H, s), 6.76 and 6.95 (each 1H, ABq, J=8 Hz).

The residue (**9**), without further purification, was dissolved in ether (50 ml) and treated with diazomethane, prepared from nitrosomethylurea (10.5 g), in ether (80 ml) at room temp for 4 h. The soln was concentrated to dryness, leaving oily residue (3.66 g), which was purified by column chromatography over silica gel (60 g). Eluates with benzene-ether (5 : 1, 150 ml) gave **9a** (3.17 g), after being dried *in vacuo* for 2 d, oil and $[\alpha]_D$ +77.2° ($CHCl_3$); MS, *m/e* 290 (M^+), 248 (M^+−CH_2CO), 216, 203, 201, 189, 160 (base), and 145; IR ($CHCl_3$), ν_{max} 1762, 1736, and 1603 cm^{-1}; NMR, δ 1.23 (3H, d, J=7 Hz), 2.00 and 2.30 (each 3H, s), 3.69 (3H, s, COOC$\underline{H}_3$), 6.74 and 6.92 (each 1H, ABq, J=8 Hz). Found: C, 70.31; H, 7.44%. Calcd for $C_{17}H_{22}O_4$: C,

70.32; H, 7.64%.

*2-(7-Hydroxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)-1-propanol (**10**) and Its Bis(p-toluenesulfonate) (**10a**).* To a suspended mixture of lithium aluminium hydride (LAH, 1.3 g) in tetrahydrofuran (THF, 100 ml) was added dropwise a soln of **9a** (2.67 g) in dry THF (35 ml) under cooling with ice. The mixture was stirred under reflux for 24 h, and cooled to 0 °C. After addition of ethyl acetate, methanol and water to decompose an excess of the reagent, the mixture was submitted to filtration to remove insoluble materials, which were washed with ethanol. The filtrate and washings were combined and evaporated to dryness, leaving an oily residue, which was shaken with ethyl acetate and 2 M hydrochloric acid. The acidic layer was washed twice with ethyl acetate. The ethyl acetate solns were combined, washed with 2 M hydrochloric acid, 5% aq sodium hydrogen carbonate and saturated brine, dried and evaporated to leave a crystalline residue (2.02 g), which on recrystallization from ethyl acetate–hexane yielded **10** (1.76 g), mp 126—127 °C and $[\alpha]_D$ +76.7°; MS, *m/e* 220 (M^+), 187, 173, 161, and 159 (base); IR, ν_{max} 3565, 3280, 1605, 1591, 1200, 1070, and 816 cm^{-1}; NMR, δ 1.00 (3H, d, J=7 Hz), 2.10 (3H, s), 3.67 (2H, m, W_H=11 Hz, $C\underline{H}_2OH$), 4.96 (1H, s, $O\underline{H}$), 6.53 and 6.76 (each 1H, ABq, J=8 Hz). Found: C, 76.33; H, 9.07%. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15%.

Compound **10** (223 mg) was treated with *p*-toluenesulfonyl chloride (446 mg) in Py (3 ml) at room temp for 40 h, and then poured into ether (100 ml). The whole soln was washed with 2 M hydrochloric acid (3×10 ml), 5% aq sodium hydrogencarbonate and saturated brine, dried and evaporated to leave an oily residue (523 mg), which was purified by column chromatography over silica gel (30 g). Eluates with benzene gave **10a** (438 mg) in pure state, oil and $[\alpha]_D$ +39.5° ($CHCl_3$); MS, *m/e* 528 (M^+), 356, 314, 313, 238, 201, 159 (base), and 157; IR ($CHCl_3$), ν_{max} 3030, 1600, 1175 (strong), 850, 832, and 815 cm^{-1}; NMR, δ 0.95 (3H, d, J=7 Hz), 1.90 (3H, s), 2.44 and 2.46 (each 3H, s, $2C\underline{H}_3C_6H_4SO_3$), 4.00 (2H, s, $C\underline{H}_2OSO_2C_6H_4CH_3$), 6.62 and 6.77 (each 1H, ABq, J=8 Hz), 7.20 and 7.72 (each 4H, m, $2CH_3C_6\underline{H}_4SO_3$).

*Conversion of **10a** into (2R)-2-Isopropyl-8-methyl-1,2,3,4-tetrahydronaphthalen-7-ol (**6**) and Its 3,5-Dinitrobenzoate (**6a**).* Compund **10a** (315 mg) in dry THF (20 ml) was treated with LAH (364 mg) under reflux for 24 h. The reaction mixture, after being cooled, was worked up as described above to leave an oily residue (131 mg), showing a single spot, which was purified by column chromatography over silica gel (6 g). Eluates with benzene yielded **6** (98 mg) in pure state, oil and $[\alpha]_D$ +85.7° ($CHCl_3$); MS, *m/e* 204 (base, M^+), 189, 161, 147, 146, 134, 122, and 121; IR (liquid), ν_{max} 3420, 1598, 1386, 1367, and 817 cm^{-1}; NMR, δ 0.98 [6H, d, J=6 Hz, $CH(C\underline{H}_3)_2$], 2.11 (3H, s, $C\underline{H}_3$ at C_8), 4.76 (1H, s, $O\underline{H}$), 6.51 and 6.75 (each 1H, ABq, J=8 Hz, 2H at C_6 and C_5).

Compound **6** (73.5 mg) was stirred with 3,5-dinitrobenzoyl chloride (112.5 mg) in dry Py (1 ml) at room temp for 16 h. The mixture was poured into ice-water (50 ml), when precipitates separated out and were collected by filtration, washed with water, 5% aq sodium carbonate and water, and dried to give a crystalline material (140 mg). This was recrystallized from acetone to give **6a** (106.5 mg), mp 159.5—160 °C and $[\alpha]_D$ +60.1° ($CHCl_3$); MS, *m/e* 398 (M^+), 368, 355, 204, 195, 186, 165 (base), 149, and 135; IR, ν_{max} 3095, 1740, 1629, 1599, 1545, 1343, 1163, 1073, 921, and 717 cm^{-1}; NMR, δ 1.01 [6H, d, J=6 Hz, $CH(C\underline{H}_3)_2$], 2.08 (3H, s, $C\underline{H}_3$ at C_8), 6.82 and 6.96 (each 1H, ABq, J=8 Hz, 2H, at C_5 and C_6), and 9.24 [3H, m, $(NO_2)_2C_6\underline{H}_3COO$]. Found: C, 63.37; H, 5.55; N, 6.82%. Calcd for $C_{21}H_{22}O_6N_2$: C, 63.31; H, 5.57; N, 7.03%.

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