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THE CONFIGURATION OF (+)-GLUTINOSONE[1)]

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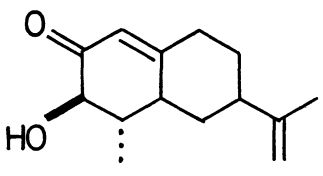
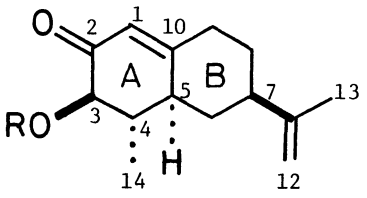
The configuration of (+)-glutinosone was determined on the basis of the chemical transformation from (-)-rishitin and the NMR spectrum in the presence of the shift reagent.

Glutinosone, an antifungal norsesquiterpene qualified as "phytoalexin" and isolated from leaves of Nicotiana glutinosa infected with tobacco mosaic virus, was assigned formula 1A by Burden and coworkers.[2)] However, the configuration of all asymmetric centers and the disposition of an isopropenyl group have not completely been determined yet. We now describe evidence that (+)-glutinosone is correctly represented by formula 1B.

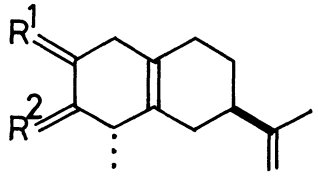
Treatment of (-)-rishitin[3)] (2) with acetic anhydride (2.3 equiv) in pyridine and benzene (1:20) (room temp, 5 h) followed by chromatography afforded the 2- and 3-monoacetates (2a and 2b), mp 60.5-62.5°C and 107-107.5°C, in 34 and 23% yields, respectively, with the 2,3-diacetate[3)] (2c) and the unreacted glycol (2) (5 and 35%): 2a,[4)] $[\alpha]_D$ -33.6°; δ 3.31 (1H, t J = 8.5 Hz, H at C_3) and 4.72 (3H, br, 3H at C_2 and C_{12}): 2b, $[\alpha]_D$ -38.9°; δ 3.62 (1H, do t J = 6.5, 8.5, and 8.5 Hz, H at C_2) and 4.60 (1H, t J = 8.5 Hz, H at C_3). The 3-monoacetate (2b), when oxidized with the Jones reagent in a heterogeneous mixture of ether and water (room temp, 21 h), was converted into the 2-dehydro compound, 2-oxo-3-acetate (3), oil, in a 61% yield: $[\alpha]_D$ +59.4°; δ 2.71 and 2.95 (each 1H, ABq J = 19 Hz, 2H at C_1) and 4.84 (1H, d J = 9 Hz, H at C_3). Treatment of compound 3 with potassium hydroxide (1.2 equiv) in methanol (room temp, 25 min) resulted in migration of the 5(10)-double bond with concomitant hydrolysis to give $\Delta^{1(10)}$-3-hydroxy-2-ketone (1B), oil, in a 46% yield, with the corresponding 3-acetate (1Ba), oil, (41%): 1B; $[\alpha]_D$



1A



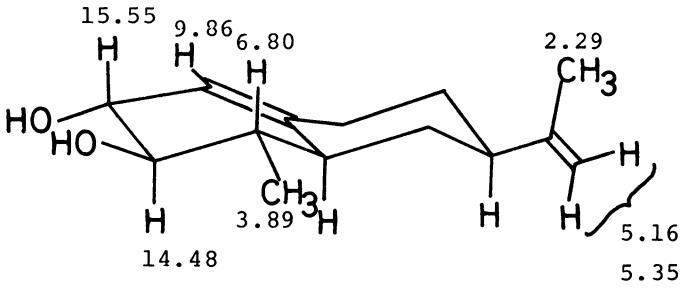
1B R=H
1Ba R=Ac



2 R^1=α-OH, β-H, R^2=α-H, β-OH
2a R^1=α-OAc, β-H, R^2=α-H, β-OH
2b R^1=α-OH, β-H, R^2=α-H, β-OAc
2c R^1=α-OAc, β-H, R^2=α-H, β-OAc
3 R^1=O, R^2=α-H, β-OAc

+57.2°; m/e 220 (M^+), 192, 191, 162, 147, 134, 121, and 94 (base); λ_{max} 237 nm (ε 14,500); ν_{max} ($CHCl_3$) 3470, 1676, 1645, 1620, and 896 cm^{-1}; δ ($CDCl_3$) 1.23 (3H, d J = 6 Hz, 14-C<u>H</u>$_3$), 1.73 (3H, s, 13-C<u>H</u>$_3$), 3.72 (1H, s, O<u>H</u>), 3.79 (1H, d J = 12 Hz, <u>H</u> at C_3), 4.72 (2H, br s W_H = 5 Hz, 2<u>H</u> at C_{12}), and 5.90 (1H, br s W_H = 4 Hz, <u>H</u> at C_1): **1Ba**, $[\alpha]_D$ +64.8°; λ_{max} 236 nm (ε 15,200); δ ($CDCl_3$) 1.12 (3H, d J = 6 Hz, 14-C<u>H</u>$_3$) and 5.11 (1H, d J = 12 Hz, <u>H</u> at C_3). All the spectra of compound **1B** were identical with those of natural glutinosone, establishing the absolute configurations at C_3, C_4 and C_7 of (+)-glutinosone (**1B**).[5,6]

Hydride reduction of (+)-glutinosone (**1B**) ($NaBH_4$ in C_2H_5OH) gave glycol[2] (**4**), mp 136-138°C, in a 56% yield: $[\alpha]_D$ -29.6°; ν_{max} ($CHCl_3$) 3580 and 3400 cm^{-1}; δ ($CDCl_3$) 1.11 (3H, d J = 6 Hz, 14-C<u>H</u>$_3$), 3.18 (1H, do d J = 10 and 8 Hz, <u>H</u> at C_3), 4.06 (1H, br d J = 8 Hz, <u>H</u> at C_2), and 5.28 (1H, br s W_H = 5 Hz, <u>H</u> at C_1). The NMR spectrum indicated that the A ring exists in a half-chair conformation.[2] Addition of 0.6 mol equiv of the shift reagent Eu(dpm)$_3$ effected complete separation of the NMR signals due to individual protons on the A ring, which were correlated to the respective signals as shown in formula **4**. Irradiation at δ 3.89 (14-C<u>H</u>$_3$) collapsed a broad multiplet at δ 6.80 (<u>H</u> at C_4) into a slightly broad <u>triplet</u> (J = 10 Hz), indicating the coupling constant between two protons at C_4 and C_5 to be 10 Hz. It follows that the proton in question at C_5 is oriented axial (α-configuration) in respect to the A ring and hence, (+)-glutinosone is correctly represented by formula **1B**.



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REFERENCES and FOOTNOTES

1) Part XV of "Studies on the Phytoalexins;" Part XIV, N. Katsui, A. Matsunaga, H. Kitahara, F. Yagihashi, A. Murai, T. Masamune, and N. Sato, Bull. Chem. Soc. Jpn., <u>50</u>, 1217 (1977).

2) R. S. Burden, J. A. Bailey, and G. G. Vincent, Phytochemistry, <u>14</u>, 221 (1975).

3) N. Katsui, A. Murai, M. Takasugi, M. Imaizumi, T. Masamune, and K. Tomiyama, J. Chem. Soc. Chem. Commun., <u>1968</u>, 43; T. Masamune, A. Murai, M. Takasugi, A. Matsunaga, N. Katsui, N. Sato, and K. Tomiyama, Bull. Chem. Soc. Jpn., <u>50</u>, 1201 (1977).

4) All compounds described herein gave elementary analyses and MS, IR, and NMR spectra in good accord with the assigned structures. The optical rotations, UV and NMR spectra were measured in ethanol, ethanol and carbon tetrachloride, respectively, unless otherwise stated. Abbreviations "s, d, t, q, br, and do" in the NMR spectra denote "singlet, doublet, triplet, quartet, broad, and double," respectively.

5) The optical rotation of glutinosone or any of its derivatives has so far been unknown; R. S. Burden (private communication, 1977).

6) We are indebted to Doctor R. S. Burden for providing us with copies of the spectra of glutinosone.

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