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3β,7β-DIHYDROXYKAURENOLIDE. A NEW METABOLITE OF GIBBERELLA FUJIKUROI

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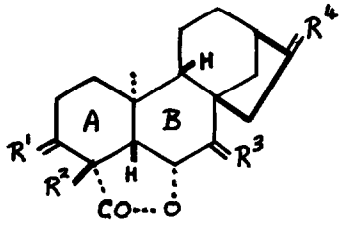
During the isolation of 7β,18-dihydroxykaurenolide[1] (1) from large scale fermentations of G. fujikuroi an isomeric metabolite [m.p. 175-176°, $[\alpha]_D^{24}$ - 34.7° (c 0.64 in $CHCl_3$)] of similar polarity was discovered which has been shown to have structure (2). Its IR spectrum revealed the presence of hydroxy, γ-lactone and terminal methylene groupings ($\nu_{max}^{CHBr_3}$ 3610, 3470, 1763, 1662 and 886 cm^{-1}), whilst the NMR spectrum [τ 8.95 (3H, s, 20-Me), 8.62 (3H, s, 18-Me), 7.95 (3H, s, OCOMe), 7.93 (3H, s, OCOMe), 5.31 (1H, t, J 6.5 Hz, 6-H), 5.12 and 5.0 (2H, br, 17-H_2), 4.6 (1H, m, 3α-H), 4.20 (1H, d, J 7 Hz, 7α-H)] of its diacetate was consistent with structure (3).

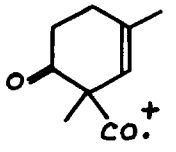
The carbon skeleton and stereochemistry (except that at C-3) of the metabolite was established by the following reaction sequence. Treatment of the monotosylate (5) with boiling collidine gave the olefin (12) which on hydrogenation afforded the tetrahydro-compound (6). Fractional crystallisation of the latter gave one of the pure 16-epimers which was identical (m.p., IR and $[\alpha]_D$) with β-dihydro-7-hydroxykaurenolide (7).[2]

Oxidation of the metabolite with chromium trioxide-pyridine-dichloromethane[3] gave the diketo-lactone (4), ν_{max} 1775 and 1700 cm^{-1}, τ 9.24 (3H, s, 20-Me), 8.44 (3H, s, 18-Me), 7.22 (d, J 7 Hz, 5-H), 5.14 (d, J 7 Hz, 6-H), 5.10 and 4.93 (17-H_2), whose mass spectrum contained peaks at m/e 151 and 123 assigned[4] to the ions (10) and (11), thus showing that ring A of the metabolite carries a secondary hydroxy-group. Reduction of the diketo-lactone (4) with chromous chloride in aqueous acetone gave inter alia the diketone (13) [$\nu_{max}^{CHBr_3}$ 1705 cm^{-1}, τ 9.02 (3H, d, J 6.5 Hz, 18-Me), 8.71 (3H, s, 20-Me), 5.06 (2H, 17-H_2)] thereby establishing that the ring A oxygen function is situated at C-3. Reduction of the diketo-lactone (4) with sodium borohydride gave the 3α,7α-diol (8) as the result of attack on the less-hindered β-face of (4) (cf. ref. 2). The chemical shift of the 5-proton doublet in the kaurenolide (2) occurs at lower field (τ 8.07) than in either 7-hydroxykaurenolide (9) (τ 8.26) or the diol (8)

(τ 8.32), thus showing that the 5-proton in (2) is deshielded by an axial (β) 3-hydroxy-group.[5]

The kaurenolide (2) is the first example of a metabolite of G. fujikuroi in which 3β-hydroxylation has occurred prior to contraction of ring B; its possible role in the biosynthesis of the gibberellins is under investigation.





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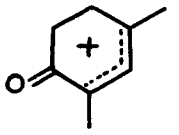

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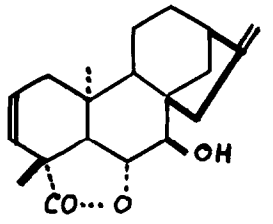
	R^1	R^2	R^3	R^4
1	H_2	CH_2OH	α-H,β-OH	H_2
2	α-H,β-OH	Me	α-H,β-OH	H_2
3	α-H,β-OAc	Me	α-H,β-OAc	H_2
4	O	Me	O	H_2
5	α-H,β-OTs	Me	α-H,β-OH	H_2
6	H_2	Me	α-H,β-OH	H,Me
7	H_2	Me	α-H,β-OH	α-Me,β-H
8	α-OH,β-H	Me	α-OH,β-H	H_2
9	H_2	Me	α-H,β-OH	H_2



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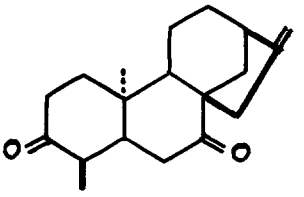

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