SYNTHESIS OF 4-*epi*-GIBBERELLIN A₁₂ FROM ENT-7 α ,18-DIHYDROXY-KAUR-16-ENE

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For some time we have been working on the partial synthesis of diterpenes, using ent-kaurene type tetracyclic diterpenes from Canary species of *Sideritis*¹ as starting material. One of our objects was the synthesis of compounds with a gibbane skeleton and in this context we carried out a cyclo B reduction via benzylic acid rearrangements². Now we have synthesized 4-*epi*-gibberellin A₁₂ from epicandicandiol³ (ent-7 α ,18-dihydroxy-kaur-16-ene)(I).

Jones' oxidation of I gave the keto-acid II which was then methylated with diazomethane yielding the methyl ester III⁴ which reacted with oxygen in Kt-BuO/t-BuOH to give the ketolactone IV in good yield (85%): mp 251-253°, [α]_D-25°, [λ]_{max} 265, ν _{max} 1792, 1675, M⁺ 312 (100%). When the acid II is auto-oxidated, the yield is lower (40%). Reduction of IV with sodium borohydride in MeOH afforded the alcohol V (80%): mp 199-201°, [α]_D-53°, δ 4.38 (s). The chloro-derivative VI: mp 200-202° (70%), was obtained by treating this alcohol with triphenyl phosphine in CCl₄/Py (9:1).

The configurations tentatively assigned to the alcohol in IV and the Cl in VI were based on the facts that reduction of the 7-oxo-kaurene derivatives gives the more stable equatorial alcohol⁴ and reaction with Ph₃P/CCl₄ takes place with inversion of configuration in most cases⁵.

When compound VI was treated with sodium methoxide in dimethoxy ethane⁶, a Favorskii rearrangement yielded 4-*epi*-gibberellin A₁₂ dimethyl ester (VII) as a gum (74%) [NMR: δ 4.86 (2H, br s), 3.62, 3.57 (3H each, 2OMe), 3.32, 2.34 (1H each, d, J=12 Hz, H₆ and H₅), 1.32 and 1.12 (3H each, s, 2Me); MS: 360, 328, 300, 285, 270, 251].

The stereochemistry of compound VII was determined on the basis of the spin coupling between the hydrogens at C₅ and C₆ (J=12 Hz) identical to that reported for the GA₁₂ dimethyl ester⁷ and for other C-20 gibberellins.

Treatment of the dimethyl ester VII with potassium t-butoxide in DMSO afforded

the 4-epi-gibberellin A₁₂ (VIII) (83%): mp 233-235°, [NMR: δ 4.85 (2H, d), 3.17, 2.36 (1H each, d, J=12 Hz), 1.40 and 1.13 (3H each, s, 2Me); MS: 314 (M⁺-18), 286, 271, 257].

To our knowledge this is the first application of the Favorskii rearrangement conditions to a chloro-enol-lactone and the first synthesis of a 4-epi-gibberellin.

R E F E R E N C E S

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- 2 González A G Fraga B M Hernández M G Larruga F and Luis J G: An Quim 71 733 (1975)
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- 4 This keto-methyl ester has also been obtained from candicandiol (ent-7β,18-dihydroxy-kaur-16-ene). See 3.
- 5 Cristol S J Strom R M and Stull D P: J Org Chem 43 1150 (1978) and references cited therein.
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- 7 Cross B E and Norton K: J Chem Soc 1570 (1965)