

TOTAL SYNTHESIS OF (-)-4-HYDROXY-2-HYDROXYMETHYL-3, α -
DIMETHYLCYCLOPENTANEETHANOL, THE IRIDANE PART OF JASMININ

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The structure (1) has been assigned to jasminin, the bitter principle isolated from Jasminium primulinum Hemsl.¹ The structure of the secoiridoid part of (1) was finally confirmed by means of alkaline hydrolysis. Mild alkaline hydrolysis of (1) gave a dicarboxylic acid (2) and a triol (3). After methylation followed by acetylation, (2) gave the tetraacetyl dimethyl ester (4), mp 116-117°, which was identified by comparison with an authentic sample derived from oleuropein.² In order to confirm the structure of the remaining iridane part of jasminin, we have synthesized the title compound (3).

The synthesis of the carbon skeleton was accomplished by Favorskii rearrangement of (+)-carvone epoxide (5).³ Treatment of (5) with sodium ethoxide yielded two hydroxy acids (6) 20% and (7) 2%, and 6-hydroxycarvone (8)⁴ 23%.

The hydroxy acid (6), mp 125-126°, $[\alpha]_D -58.7^\circ$ (EtOH), shows NMR signals (δ CDCl₃-d₆DMSO) at 1.10 (3H, d, J=6 Hz), 1.72 (3H, s), 1.85 (2H, m, H₅, H₅'), 2.15 (1H, m, H₃), 2.21 (1H, t, J=9 Hz, H₂), 3.06 (1H, ddd, J=9, 9 and 10 Hz, H₁), 3.75 (1H, ddd, J=5, 6 and 6 Hz, H₄) and 4.72 ppm (2H, m, olefinic protons). These NMR assignments were supported by decoupling experiments. The acid (6) gave a methyl ester (9), bp 81-82°/0.15 Torr, alkaline hydrolysis of which yielded the starting material.

The structure (7) was assigned to the second product on the basis of NMR evidence and mechanistic grounds⁵ [cleavage at b of the intermediate (10)].

The third product was found to be 6-hydroxycarvone on the basis of physical

data. And it was confirmed by the following transformation. Methylation of (8) with diazomethane, reduction with sodium dihydro-bis(2-methoxyethoxy)aluminate followed by acid treatment gave dl-carvone.

Oxidation of the methyl ester (9) with Jones' reagent gave the keto ester (11), which afforded, on catalytic reduction, a dihydro keto ester (12). This shows a strong negative Cotton effect curve, which suggests the absolute configuration as shown in the formula.⁶ The same compound had already been derived from jasminin¹ and the identity was confirmed by direct comparison.

The remaining problem is on the stereochemistry of the secondary alcohol of (6). The assignment of configuration of (6) is based (a) on mechanistic grounds⁵ [cleavage at a of the intermediate (10)] and (b) on NMR evidence ($J_{4,5\alpha}=5$ Hz, $J_{4,5\beta}=5$ Hz, $J_{3,4}=6$ Hz). Reduction of (11) with NaBH_4 gave (9).

Hydroboration of (9) gave the triol (3). This completes a new total synthesis of the title compound. Its acetate (13), bp $126^\circ/0.18$ Torr, $[\alpha]_D^{25} -22.5^\circ$ (CHCl_3), was spectroscopically and chromatographically identical with the triacetate derived from jasminin.¹ The monoacetate (14), available for the total synthesis of jasminin, was synthesized by the following sequence of reactions: (a) reduction of (9) with sodium dihydro-bis(2-methoxyethoxy)aluminate, (b) benzylation, (c) hydroboration, (d) acetylation and (e) catalytic debenylation.

Satisfactory analytical and spectroscopic data were obtained for all new compounds.

References

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