Tetrahedron Letters No.9, pp. 1111-1112, 1968. Pergamon Press. Printed in Great Britain.

INSECT HORMONES, VI. CONFIRMATION OF THE SKELETAL STRUCTURE OF PONASTERONE A[1][*]

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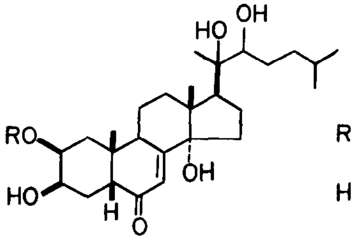
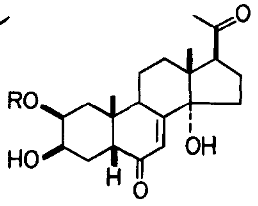
Structure 1 was assigned to ponasterone A mainly on the basis of the physico-chemical data of ponasterone A and three derivatives[2]. The stereochemical deduction was partially based on comparisons of the NMR chemical shifts of the methyl peaks of ponasterone A with ecdysone, the structure of which had been established by X-ray studies[3] and by synthesis[4,5]. However, the NMR data compared were those measured in pyridine which, due to its strong solvating power and anisotropic effect, is not necessarily an ideal solvent for such purposes. Moreover, ring A can adopt a twist-boat conformation, especially so in the present case of a ring A/B cis steroid, and this would introduce an additional complicating factor. Accordingly, a direct chemical correlation between ponasterone A and an authentic sample was necessary in order to establish the configurations at the various asymmetric centers of the nucleus, and this has been achieved in the following manner.



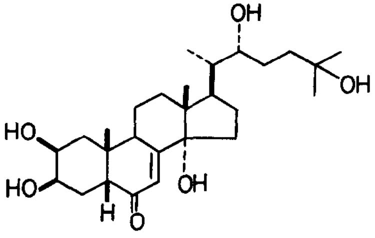
1 R=H

2 R=Ac



3 R=Ac

4 R=H



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Acetylation of ponasterone A (200 mg) employing ten equivalents of acetic anhydride (0.5 ml) in a large volume of pyridine (4 ml) and dichloromethane (10 ml) for 20 hours at 0° gave selectively 2-acetylponasterone A (2), m.p. 222-223° (needles from ether) in 55% yield; NMR (CDCl$_3$): 0.87 (3H, s, 18-Me), 0.91 (6H, d, J=6, 26/27-Me), 0.99 (3H, s, 19-Me), 1.20 (3H, s, 21-Me). The two carbinyl protons in the A ring of ponasterone A derivatives (and other similar steroids such as ecdysterone) are readily differentiated since the NMR half-band width ($W\frac{1}{2}$) of one of them, which is involved in an axial-axial coupling with an adjacent methylene proton, is ca 20 cps, whereas that of the other is 7-12 cps. Provided ponasterone A is an A/B cis steroid having 2β, 3β-hydroxyl groups (confirmed below), the 2α-axial proton is the one with the larger $W\frac{1}{2}$. The monoacetate 2 had a peak at 5. 00 ppm (AcO-C-H) with $W\frac{1}{2}$ 20 cps and therefore it is the 2-acetate.

Oxidation of 2-acetylponasterone A (2) with sodium periodate in aqueous ethanol gave the methyl ketone 3, m. p. 231-232° (cubes from ether-dichloromethane), IR ($CHCl_3$): 3600, 3400, 1740 (OAc), 1705 (20-one), 1660 cm^{-1} (6-one); NMR ($CDCl_3$): 0. 63 (3H, s, 18-Me), 0. 99 (3H, s, 19-Me), 2. 09 (3H, s, 2-OAc), 2. 15 (3H, s, 21-Me), 4. 15 (1H, m, $W\frac{1}{2}$ 7 cps, C_3-H), 5. 00 (1H, m, $W\frac{1}{2}$ 20 cps, C_2-H), and 5. 85 ppm (br, s, C_7-H).

Hydrolysis of the methyl ketone under controlled conditions (10 mg of 3/5 mg of $KHCO_3$/ 4 ml of 85% aqueous methanol/12 hrs at room temperature under N_2) yielded in quantitative amount the hydrolysed methyl ketone 4, identical (TLC, IR in KBr disk) with an authentic specimen$^{6)}$ which was produced during the course of ecdysone (5) synthesis$^{4, 7)}$.

Very recently the skeletal structure of crustecdysone has also been shown to be identical with that of ecdysone$^{7)}$.

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6) We are grateful to Dr. J. Fried, Syntex Corporation, for providing us 1 mg of this precious sample and the IR chart.

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