EXPERIENTIA

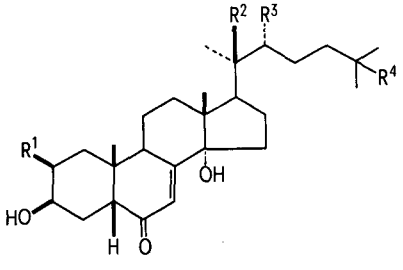
Vol. 31 – Fasc. 8 Pag. 873 – 1000 15. 8. 1975

SPECIALIA

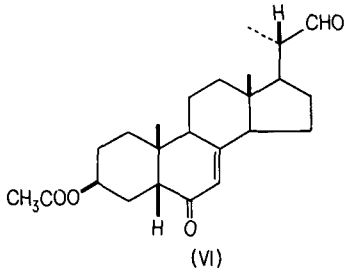
Insect Moulting Hormones: Synthesis and Biological Activity of 2,25-Dideoxy-α-Ecdysone and Deoxyecdysone

The 2-deoxy ecdysone analogues deoxyecdysone (I) and deoxycrustecdysone (II) show[1] the same biological activity as β-ecdysone (III) in the *Calliphora* bioassay using abdomens of *C. stygia*[2]. The same activity is also shown by the 25-deoxy compound ponasterone A (IV), while other known deoxy analogues are all of lesser activity[3]. These data suggest that 2,25-dideoxy-α-ecdysone (V) should have all the hydroxy groups necessary for maximum activity in the bioassay. It was thus of interest to synthesize compound (V) in order to determine its activity and possible effects on moulting and metamorphosis. A variation of the synthetic route used gave deoxyecdysone, and provided a final proof of structure for this compound.

Ergosteryl acetate was converted by known methods[4], involving chromic acid oxidation, zinc-acetic acid reduction and ozonolysis, to the 5β-aldehyde (VI). Yields of the required 5β-epimer after the reduction step were improved by equilibration of the 5α-epimer in refluxing acetic acid. Compound (VI) was then alkylated with a reagent prepared from 3-methylbut-1-yne and methyl lithium in ether-tetrahydrofuran at –30 °C, and afforded a mixture of 22R- and 22S-epimers in roughly equal proportions. Partial hydrolysis of the 3-acetoxy group occurred during the reaction, as well as some epimerization at C-5. The required 3β,22R-dihydroxy-5β-cholest-7-en-23-yn-6-one, isolated by chromatography of the reaction mixture, was hydrogenated over platinum and the unstable product immediately reacted with selenium dioxide in dioxan to introduce the 14-hydroxy group. After purification 2,25-dideoxy-α-ecdysone (V) was obtained as colourless plates, m.p. 260–266°, λ_{max} (ethanol) 243 nm (13,500), $\nu_{max.}$ (KBr) 3450 and 1640 cm^{-1}, methyl resonances, δ(py-d_5) 0.75 (s, C-18), 0.85 (d, J 6 Hz, C-26,27), 1.07 (s, C-19), 1.28 ppm (d, J 6 Hz, C-21). The correctness of the structural assignment was verified by comparison of UV-, IR- and PMR-spectra with those of known analogues. Assignment of the 22-configuration was facilitated by comparison of C-18 methyl proton solvent shifts with those of model compounds. The difference in chemical shift of the C-18 methyl group for pyridine and methanol solvents was 0.02 ± 0.01 ppm for the 22R-epimers, and 0.12 ± 0.03 ppm for the 22S-epimers.



	R^1	R^2	R^3	R^4
(I)	H	H	OH	OH
(II)	H	OH	OH	OH
(III)	OH	OH	OH	OH
(IV)	OH	OH	OH	H
(V)	H	H	OH	H



(VI)

Synthesis of deoxyecdysone followed a similar pattern, with 3-methyl-3-tetrahydropyranyloxybut-1-yne being used in the alkylation step. The synthetic compound, m.p. 230–233°, showed spectroscopic properties identical with those[1] of the natural material and the mixed m.p. was undepressed. Biological activity of the synthetic deoxyecdysone in the *Calliphora* test was the same as that of the natural material, and equal to that of β-ecdysone.

By contrast, the activity of 2,25-dideoxy-α-ecdysone was only half that of β-ecdysone and very little greater than that of 2,22,25-trideoxy-α-ecdysone (VI).

Résumé. Le 2,25-didéoxy-α-ecdysone et le déoxyecdysone out été préparés à partir de l'acétate d'ergostéryl. Dans l'essai biologique sur le *Calliphora* le didéoxy-α-ecdysone est la moitié moins actif que le β-ecdysone.

M. N. Galbraith, D. H. S. Horn and J. A. Thomson

Division of Applied Organic Chemistry, C.S.I.R.O., Box 4331 G.P.O., Melbourne 3001 (Australia), and Department of Genetics, University of Melbourne, Parkville, Victoria 3052 (Australia), 24 March 1975.

[1] Y. K. Chong, M. N. Galbraith and D. H. S. Horn, Chem. Commun. *1970*, 1217.

[2] J. A. Thomson, F. P. Imray and D. H. S. Horn, Aust. J. exp. Biol. Med. Sci. *48*, 321 (1970).

[3] M. N. Galbraith, D. H. S. Horn, E. J. Middleton and J. A. Thomson, Experientia *29*, 19 (1973).

[4] A. Furlenmeier, A. Fürst, A. Langemann, G. Waldvogel, P. Hocks and R. Wiechert, Helv. chim. Acta, *50*, 2387 (1967). – W. B. Smith and G. P. Newsoroff, Steroids *22*, 819 (1973).