Synthetic Studies on Insect Hormones.[1] The Synthesis of a Possible Metabolite of Crustecdysone (20-Hydroxyecdysone)

By J. B. SIDDALL*

(*Institute of Steroid Chemistry, Syntex Research, Palo Alto, California*)

and D. H. S. HORN and E. J. MIDDLETON

(*Division of Applied Chemistry, C.S.I.R.O. Melbourne, Australia*)

THE suggestion[2] that crustecdysone (20-hydroxyecdysone) (Ib), an insect-moulting hormone, may undergo biological side-chain cleavage to 2β,3β,-14α-trihydroxy-5β-pregn-7-ene-6,20-dione (II) has prompted its synthesis, and two routes to this compound are now reported.

The synthesis of the insect-moulting hormone ecdysone (Ia) was described[3] by a Syntex group. Along with three stereoisomers of ecydsone, there was obtained a by-product† lacking the cholestane side-chain and thought to be a 23-norcholane derivative.

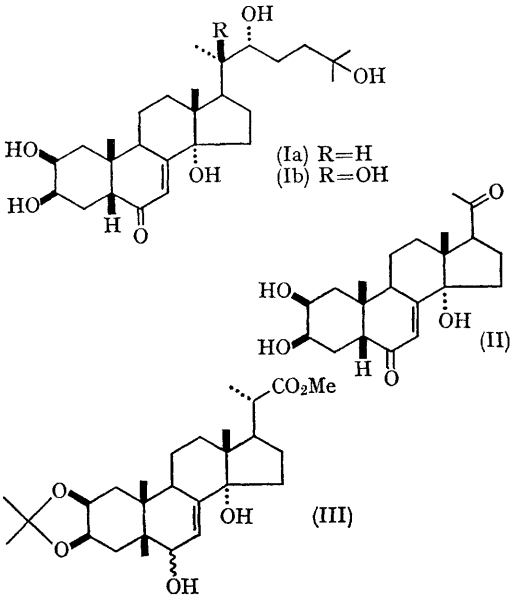
We are now able to report the structure of this by-product as 2β,3β,14α-trihydroxy-5β-pregn-7-ene-6,20-dione (II) which probably arose from base-catalysed α-oxygenation followed by cleavage of the methoxycarbonyl group of the alkylation substrate[3] (III). Subsequent reduction and re-oxidation[3] (MnO_2) could regenerate[4] the 20-carbonyl group.

The structure of (II) (m.p. 232—235°) is evident from the n.m.r. spectrum‡ (perdeuteropyridine) [δ 0·68 (18-H), 1·00 (19-H), 2·12 (21-H), 4·05 (multiplet, 2β-H), 4·19 (multiplet, 3α-H), 5·90 and 5·97 (OH), 6·15 (doublet, J = 2·5, 7-H) and 6·53 p.p.m. (14α-OH)] and mass spectrum‡ [362 (M^+),

† Fraction D mentioned in reference 3.

‡ N.m.r. spectra were recorded on a Varian H.A-100 spectrometer using Me_4Si as internal standard. Mass spectra were measured on an Atlas CH-4 instrument using a direct inlet system.

344 ($M-H_2O$), 326 ($M-2H_2O$), 301 ($M-H_2O-CH_3CO$), 283 ($M-2H_2O-CH_3CO$)]. Infrared



spectra [ν_{max}(KBr) 1647, 1700] showed the presence of a saturated carbonyl group in addition to the $\alpha\beta$-unsaturated-6-ketone [λ_{max}(EtOH) 240 mμ (ϵ = 12,400). Found: C, 69·8; H, 8·5%].

The ketone (II) has also been obtained by oxidation of crustecdysone (Ib) (m.p. 241—242·5°) from *Podocarpus elatus*[5] with a 1:1 mixture of aqueous sodium metaperiodate and pentanol at pH 7. The product after chromatographic purification (m.p. 230—233° from acetone) did not depress the melting point of the synthetic material (m.p. 232—235°) and gave identical infrared and mass spectra. The tetracycles of ecdysone and crustecdysone are thus shown to be identical.

The ketone (II) was inactive in the *Calliphora* test for insect-moulting hormone activity, but injection of an aqueous solution of (II) into the brainless pupae of the silk moth *Samia cynthia* initiated adult development at four times the dose required for ecdysone.

A careful search through the extracts of one ton of crayfish failed to reveal the presence of (II). It now seems likely that crustecdysone does not follow a degradation sequence[6] analogous to cholesterol.

(*Received, July 21st*, 1967; *Com.* 752.)

[1] For previous papers see I. T. Harrison, J. B. Siddall, and J. H. Fried, *Tetrahedron Letters*, 1966, 3457, and P. Crabbé, A. Cruz, and J. Iriarte, *Chem. and Ind.*, submitted for publication.
[2] D. H. S. Horn, E. J. Middleton, J. A. Wunderlich, and F. Hampshire, *Chem. Comm.*, 1966, 339.
[3] J. B. Siddall, A. D. Cross, and J. H. Fried, *J. Amer. Chem. Soc.*, 1966, **88**, 862.
[4] Oxidation of saturated alcohols by MnO_2 has been reported by I. T. Harrison, *Proc. Chem. Soc.*, 1964, 110.
[5] G. N. Galbraith and D. H. S. Horn, *Chem. Comm.*, 1966, 905.
[6] K. Shimizu, M. Gut, and R. I. Dorfman, *J. Biol. Chem.*, 1962, **237**, 699.