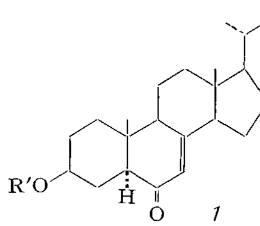
SPECIALIA

The Synthesis of Ecdysone[1]

Recently, the synthesis of ecdysone, an insect moulting hormone, has been announced by two different research groups[2,3]. Both these syntheses require over 20 stages starting from readily available steroids.

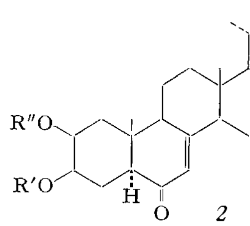
We wish to communicate a second synthesis which furnished ecdysone in 14 stages starting from ergosterol. Oxidation of ergosterol acetate with chromic acid followed by a reduction of the product with zinc in acetic acid gave the known compound *1a*[4].



1

a) R = C_7H_{13}, R′ = Ac

b) R = C_7H_{13}, R′ = Mes

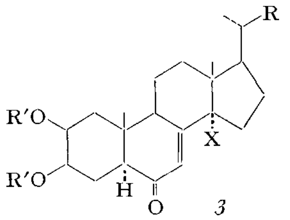


2

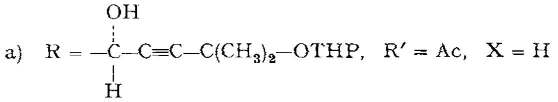
a) R = C_7H_{13}, R′ = H, R″ = Ac

b) R = C_7H_{13}, R′ = R″ = Ac

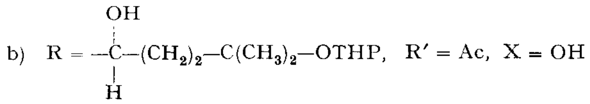
c) R = CHO, R′ = R″ = Ac



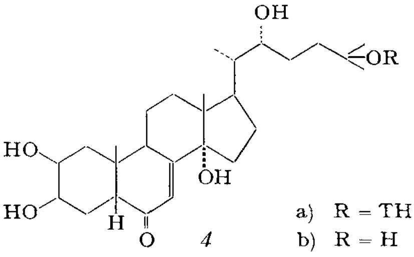
3



a) $R = -\overset{\overset{\displaystyle OH}{\vdots}}{\underset{\underset{\displaystyle H}{|}}{C}}-C{\equiv}C-C(CH_3)_2-OTHP$, R′ = Ac, X = H



b) $R = -\overset{\overset{\displaystyle OH}{\vdots}}{\underset{\underset{\displaystyle H}{|}}{C}}-(CH_2)_2-C(CH_3)_2-OTHP$, R′ = Ac, X = OH



4

a) R = THP

b) R = H

This could be hydrolysed to the corresponding alcohol and re-esterified with mesylchloride to give 3β-mesyloxy-5α-ergosta-7,22-dien-6-one *1b*. Elimination of methanesulphonic acid led to the Δ^2-olefine (m.p. 153°; $\nu_{H-2,3}$ 5.63 ppm[5]). The structure of this compound was also ascertained by mass spectrometry (fragment 340 was obtained with a high intensity). Stereospecific introduction of the *cis*-β-glycol function with silver acetate and iodine in moist acetic acid[6] furnished the monoacetate *2a* which was converted by conventional methods to the diacetate *2b* (m.p. 195–196°; ν_{H-19} 1.00 ppm). The ergosterol side chain was removed by ozonization and reductive cleavage of the ozonide gave the aldehyde *2c* (m.p. 211–212°; ε_{243} = 13,700; ν_{H-18} 0.65 ppm; ν_{H-21} 1.15 d ppm; $[\alpha]_{589}^{25°}$ + 40°). Condensation of this aldehyde with the Grignard reagent prepared from 2-methyl-3-butin-2-ol tetrahydropyranyl ether led to a mixture of diastereomers[2] with the desired 22*R*-component *3a* preponderating, which could be separated by column chromatography (m.p. 188°; ν_{H-18} 0.63 ppm, ν_{H-21} 1.08 d ppm, ν_{H-22} 4.47 d ppm; $[\alpha]_{589}^{25°}$ + 36°). The 14α-hydroxyl group was introduced by reaction with selenium dioxide in dioxane[6] after catalytic reduction of the triple bond[2] to yield the dihydroxy-compound *3b* (m.p. 194–195°; ε_{240} = 12,700; ν_{H-18} 0.69 ppm; ν_{H-7} 5.91 d ppm; $[\alpha]_{589}^{25°}$ + 66°).

Equilibration under mild alkaline conditions[7] furnished the free 5β-glycol *4a*, and by removal of the tetrahydropyranyl ether grouping with dilute hydrochloride acid ecdysone *4b* was obtained (m.p. 241° (dec.); ε_{242} = 12,400; ν_{H-18}^{DMSO} 0.63 ppm, $\nu_{H-19+20}^{DMSO}$ 0.85 ppm, ν_{H-25}^{DMSO} 1.08 ppm; $[\alpha]_{589}^{25°}$ + 76°). The material was identical in all physical properties with that reported earlier[2] and showed the required biological activity in the *Calliphora*-test.

Zusammenfassung. Ecdyson, ein Häutungshormon der Insekten, wurde ausgehend von Ergosterin in 14 Stufen synthetisiert. Wesentliche Zwischenprodukte waren (20*S*)-2β,3β-Diacetoxy-20-formyl-5α-pregn-7-en-6-on und (22*R*)-2β,3β-Diacetoxy-14,22-dihydroxy-25-(tetrahydropyran-2-yloxy)-5α-cholest-7-en-6-on.

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[1] Part VIII on insect hormones. Part VII see Proc. 2nd Intern. Congr. Steroid Hormones, Milan, 1966; Part VI see Angew. Chem. *78*, 680 (1966).

[2] U. Kerb, G. Schulz, P. Hocks, R. Wiechert, A. Furlenmeier, A. Fürst, A. Langemann, and G. Waldvogel, Helv. chim. Acta *49*, 1601 (1966).

[3] J. B. Siddall, A. D. Cross, and J. H. Fried, J. Amer. chem. Soc. *88*, 862 (1966).

[4] D. H. R. Barton and C. H. Robinson, J. chem. Soc. *1954*, 3045.

[5] NMR-spectra were recorded on a Varian HA-100 spectrometer using deuterochloroform as solvent when possible.

[6] A. Furlenmeier, A. Fürst, A. Langemann, G. Waldvogel, U. Kerb, P. Hocks, and R. Wiechert, Helv. chim. Acta *49*, 1591 (1966).

[7] J. B. Siddall, S. P. Marshall, A. Bowers, A. D. Cross, J. A. Edwards, and J. H. Fried, J. Am. chem. Soc. *88*, 379 (1966).