

## Unsaturated Steroids. Part 7.<sup>1</sup> A Simple Synthesis of 22,23-Dihydroergosterol

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From the acetate (1) of ergosterol epidioxide, 22,23-dihydroergosterol is available, by a short series of transformations in high yield.

THE first description of 22,23-dihydroergosterol was recorded in 1934.<sup>2</sup> No satisfactory preparative route to this compound was reported, however, until recently,<sup>3,4</sup> despite its potential as a pre-vitamin D, and its important role in certain biosynthetic pathways.<sup>5</sup> We now report a route simpler and more appropriate for large-scale preparative work than those already available.<sup>3,4</sup>

Hydrogenation (over platinic oxide in *pure* ethyl acetate containing suspended potassium carbonate) of the now readily<sup>6</sup> available epidioxide (1) of ergosteryl acetate afforded ergostane-3 $\beta$ ,5 $\alpha$ ,8 $\alpha$ -triol 3-acetate (2) in high yield without side reactions (contrast ref. 7). The acid-catalysed dehydration of (2) to give the 7-ene (3), in indifferent yield, has been reported previously.<sup>7-9</sup> Our extensive reinvestigation of this step has established its complexity; however, the use of hydrochloric acid-methanol, under carefully defined conditions, achieves the conversion of (2) into (3) almost instantaneously, in a reproducible yield of 40–50%. Longer reaction times

(contrast the work of Bogoslovskii *et al.*,<sup>8,9</sup> which became available to us during our investigation and which, in our hands, has been irreproducible, and that of Jones *et al.*<sup>7</sup>) rapidly diminish the yield of (3) and greatly increase the difficulty of isolating it from the complex resultant mixture of dehydration-isomerisation products. Dehydration of the 7-ene (3) occurred with thionyl chloride-pyridine (*cf.* ref. 3) to give (in >90% yield) 22,23-dihydroergosteryl acetate.

This process, which we have employed to make 22,23-dihydroergosterol in quantity for other work has been potentially available for some time, but the relative inaccessibility of the epidioxide (1) prior to 1974 (ref. 5) together with the technical difficulties of converting (1) into (2) and (2) into (3) in high yield have prevented its realisation.

### EXPERIMENTAL

*Ergostane-3 $\beta$ ,5 $\alpha$ ,8 $\alpha$ -triol 3-Acetate (2).*—A solution of 3 $\beta$ -acetoxy-5 $\alpha$ ,8 $\alpha$ -peroxyergosta-6,22-diene<sup>6</sup> (2 g) in ethyl

<sup>1</sup> Part 6, A. Emke, D. Hands, J. M. Midgley, W. B. Whalley, and R. Ahmad, *J.C.S. Perkin I*, preceding paper.

<sup>2</sup> A. Windaus and R. Langer, *Annalen*, 1934, **508**, 105.

<sup>3</sup> J. Brynjolfsson, D. Hands, J. M. Midgley, and W. B. Whalley, *J.C.S. Perkin I*, 1976, 826.

<sup>4</sup> D. H. R. Barton, A. A. L. Gunatilaka, T. Nakanishi, H. Patin, D. A. Widdowson, and B. R. Worth, *J.C.S. Perkin I*, 1976, 821.

<sup>5</sup> D. H. R. Barton, J. E. T. Corrie, D. A. Widdowson, M. Bard, and R. A. Woods, *J.C.S. Perkin I*, 1974, 1326.

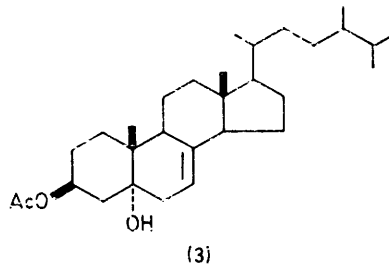
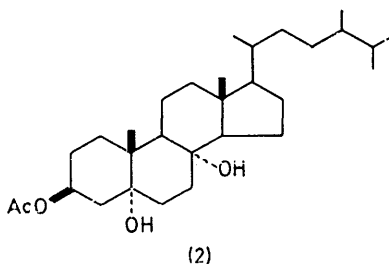
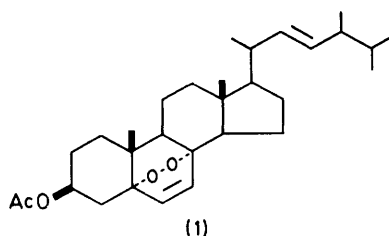
<sup>6</sup> D. H. R. Barton, G. Leclerc, P. D. Magnus, and I. D. Menzies, *J.C.S. Chem. Comm.*, 1972, 447.

<sup>7</sup> R. B. Clayton, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 1953, 2015.

<sup>8</sup> N. A. Bogoslovskii, S. S. Levi, R. P. Evstigneeva, N. P. Lazareva, and E. A. Petrova, *Khim.-Farm. Zhur.*, 1974, **8**, 44.

<sup>9</sup> N. A. Bogoslovskii, S. S. Levi, R. P. Evstigneeva, and G. I. Samokhvalov, *Zhur. obshchei Khim.*, 1975, **45**, 925.

acetate (100 ml) (which had been distilled and stored over potassium carbonate) containing potassium carbonate (50 mg) and prehydrogenated platinum oxide (0.5 g) was shaken



in hydrogen during 2 h; 3 equiv. (286 ml) had then been absorbed. The filtered solution was evaporated *in vacuo* below 40 °C to give the acetoxy-diol, which formed needles (1.8 g) (from methanol), m.p. 165–195° (decomp.) (lit.,<sup>7</sup> 170–200°),  $[\alpha]_D^{22} -40.5^\circ$  (*c* 0.93 in  $\text{CHCl}_3$ ) {lit.,<sup>7</sup>  $[\alpha]_D -43^\circ$  (*c* 0.72 in  $\text{CHCl}_3$ )} (Found: C, 75.5; H, 11.2. Calc. for  $\text{C}_{30}\text{H}_{52}\text{O}_4$ : C, 75.6; H, 11.0%),  $\nu_{\text{max.}}$  ( $\text{CHCl}_3$ ) 3 220 (OH) and 1 724  $\text{cm}^{-1}$  (OAc).

**Ergosta-5,7-dien-3β-yl Acetate.**—A solution of the foregoing acetoxy-diol (1 g) in methanol (75 ml) was maintained at 25 °C, while 10N hydrochloric acid (10 drops) in methanol (10 ml) was introduced *as rapidly as possible* to the well stirred solution. The resultant mixture was immediately added *as rapidly as possible* to a vigorously stirred saturated solution of sodium hydrogen carbonate (200 ml). These conditions are critical! The precipitate was collected, washed with water, dried, and purified from acetone to yield ergost-7-ene-3β,5α-diol 3-acetate (0.42 g, 42%) in plates, m.p. 220–222° (lit.,<sup>7</sup> m.p. 224–229°),  $[\alpha]_D^{22} +17.5^\circ$  (*c* 5.6 in  $\text{CHCl}_3$ ) {lit.,<sup>7</sup>  $[\alpha]_D^{23} +15.2^\circ$  (*c* 2.0 in  $\text{CHCl}_3$ )},  $\nu_{\text{max.}}$  ( $\text{CHCl}_3$ ) 3 460 (OH) and 1 767  $\text{cm}^{-1}$  (OAc),  $\tau$  4.62–5.12 (1 H, m, H-3α) and 4.82–4.95 (1 H, m, H-7) (Found: C, 78.8; H, 11.2. Calc. for  $\text{C}_{30}\text{H}_{50}\text{O}_3$ : C, 78.6; H, 11.0%), identical with a specimen prepared by an alternative method,<sup>4</sup> and converted as described<sup>4</sup> into ergosta-5,7-dien-3β-yl acetate.

We thank Professor Sir Derek Barton for a copy of his manuscript<sup>4</sup> prior to publication, and Glaxo Research Limited for financial assistance. The work was carried out by (D. J. C.) and by (R. W.) during the tenure of Teaching Fellowships.

[6/1120 Received, 11th June, 1976]