Synthesis of Rings A and B of Strophanthidin

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A NUMBER of steroidal cardiac-active principles[1] contain an oxygen atom at the 19-position and hydroxyl groups in the 3β- and 5β-positions. A typical member of this class of cardiac-active principles is strophanthidin. In this communication we describe the first successful attempt at the construction of rings A and B of strophanthidin.

19-Oxocholesterol[2] (I) on treatment with methanolic hydrogen chloride gave the cyclic ether[3] (II; 90%). This on epoxidation with *m*-chloroperbenzoic acid gave the 5α,6α-oxide (III; 67%), which on treatment with lithium aluminium hydride gave the 5α-alcohol (IV; 74%). The latter was recovered unchanged when treated with chromium trioxide and pyridine. The 5α-alcohol (IV) was hydrolysed with aqueous perchloric acid in dioxan to furnish the dihydroxy-aldehyde (V; 72%). This on equilibration with methanolic potassium hydroxide gave a mixture of (VII) and (V) in the ratio 1·5 : 1. Chromatography of the mixture gave 19-oxocoprostane-3β,5β-diol (VII; 50%). The structure of (VII) was proved by the fact that it is less polar than (V) and that on treatment with methanolic hydrogen chloride (VII) gave the cyclic ether (II) in high yield. Treatment of 19-oxocoprostane-3β,5β-diol (VII) with methanolic potassium hydroxide gave the same equilibrium mixture as is obtained from its precursor, the 5α-epimer. It is suggested that the transformation takes place through the intermediacy of (VI).

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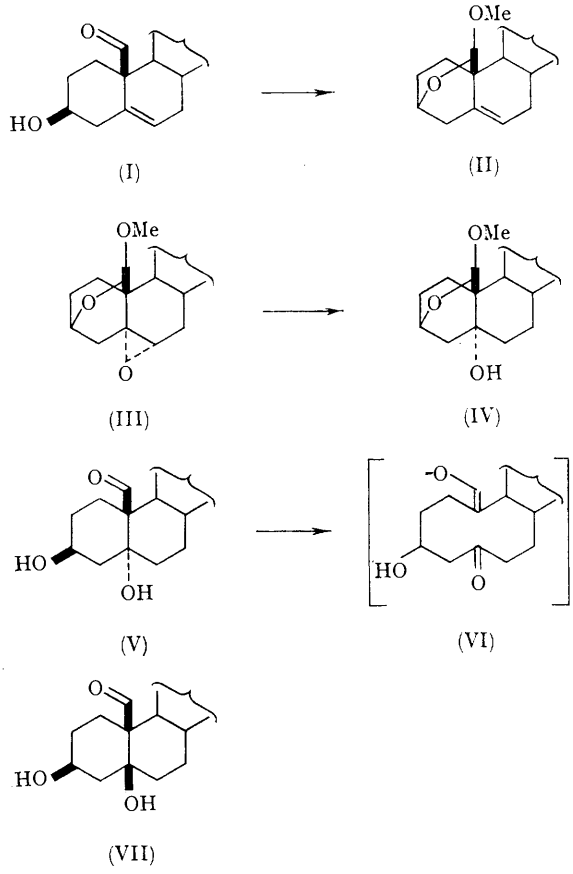

[1] The subject is reviewed by L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, 1959.
[2] M. Akhtar and D. H. R. Barton, *J. Amer. Chem. Soc.*, 1963, **86**, 1528.
[3] See also R. M. Moriarty and T. D. J. D'Silva, *Tetrahedron*, 1965, **21**, 547.