

DEGRADATION OF THE LANOSTEROL SIDE-CHAIN

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(Received in UK 16 February 1970; accepted for publication 26 February 1970)

Recent<sup>1</sup> reports on the degradation of bile acid side-chains have prompted us to record our own with the lanosterol side-chain. Mild degradation of 3 $\beta$ -acetoxy lanost-8,24-diene (I) to an equilibrium mixture of 3 $\beta$ -acetoxy-4,4,14 $\alpha$ -trimethylpregn-8- and 7-en-20-one (VIII) has been achieved as follows.

Epoxidation of (I) with monoperphthalic acid gave (II), m.p. 175-9<sup>o</sup> (90%);  $\delta$  2.70 (m, IH, C-24), 1.28 and 1.30 (2s, 6H, C-26 and C-27). Treatment of (II) in benzene with BF<sub>3</sub> etherate produced, as the major product (70%), the keto acetate (IV), m.p. 122-26<sup>o</sup>,  $\nu_{\max}$  1730 (acetate C=O), 1717 cm<sup>-1</sup> (saturated C=O);  $\delta$  1.06 (septet, J = 7 Hz, IH, C-25). The minor product was the aldehyde (III), m.p. 121-3<sup>o</sup>;  $\nu_{\max}$  2720 cm<sup>-1</sup> (aldehyde C-H);  $\delta$  1.04 (s, 6H, C-26 and C-27), 9.16 (s, IH, -CH=O). The keto acetate (IV) could be separated from the aldehyde by oxidation of the mixture with Jones reagent and extraction of the acid (IIIa).

Reaction of (IV) with 2 moles of Br<sub>2</sub> - HOAc followed by stirring in the presence of HBr for 30 min gave the dibromo compound (V), m.p. 215-218<sup>o</sup> (80%);  $\nu_{\max}$  1735 cm<sup>-1</sup> (acetate and  $\alpha$ -bromo ketone C=O);  $\delta$  5.18 (d, J = 14 Hz, IH, C-23).

Treatment of (V) with LiBr-Li<sub>2</sub>CO<sub>3</sub> in DMF at 110<sup>o</sup> produced the dienone (VI), m.p. 179-82<sup>o</sup> (67%);  $\nu_{\max}$  1665 (conjugated C=O), 1610 cm<sup>-1</sup> (C=C);  $\lambda_{\max}$  244 m $\mu$  ( $\epsilon$  13,100);  $\delta$  1.92 (s, 3H, C-26). The n.m.r. spectra of (VI) and the sequential compounds VII - IX indicate a mixture of  $\Delta^7$  and  $\Delta^8$  isomers.<sup>2</sup>

Attempted preparation of the morpholine or pyrrolidine enamines (VII) gave orange oils which were only 50% pure (t.l.c.). Ozonolysis of the crude mixture gave a large amount of polymeric material but preparative t.l.c. of the mixture afforded a 10% yield [based on (VI)] of (VIII), m.p. 166-69<sup>o</sup>;  $\nu_{\max}$  1725 (acetate C=O), 1710 cm<sup>-1</sup> (saturated C=O);  $\delta$  2.15 (s, 3H, C-21). An alternative synthesis of (VIII) was achieved via the oxidation (KMnO<sub>4</sub>) of (VI) to the aldehyde (IX) [m.p. 110-111<sup>o</sup>;  $\nu_{\max}$  2720 cm<sup>-1</sup> (aldehyde C-H);  $\delta$  9.31 (d, J = 3Hz, IH, C-22); M.S. 414,356] and further oxidation with oxygen in the presence of Cu<sup>2+</sup> and pyridine.<sup>3</sup>

In spite of the low yield in the last step (I) has been converted to (VIII) in 3% overall yield and the method is superior to the Barbier-Wieland method<sup>4</sup> which not only gives low yields but also introduces oxygen functions into rings B and C. Attempts are being made to optimize the yields in the last step.

All n.m.r. data were measured in  $\text{CDCl}_3$ , i.r. data in  $\text{CHCl}_3$  and all compounds gave satisfactory analytical figures.

**Acknowledgement:** The award of a Research Fellowship (to J.P.B.) by the New Zealand Wool Research Organisation is gratefully acknowledged.

## REFERENCES

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