

## Reactions of Epoxides. A "Back-bone" Rearrangement of 3 $\beta$ -Acetoxy-5,6 $\alpha$ -epoxy-5 $\alpha$ -cholestane

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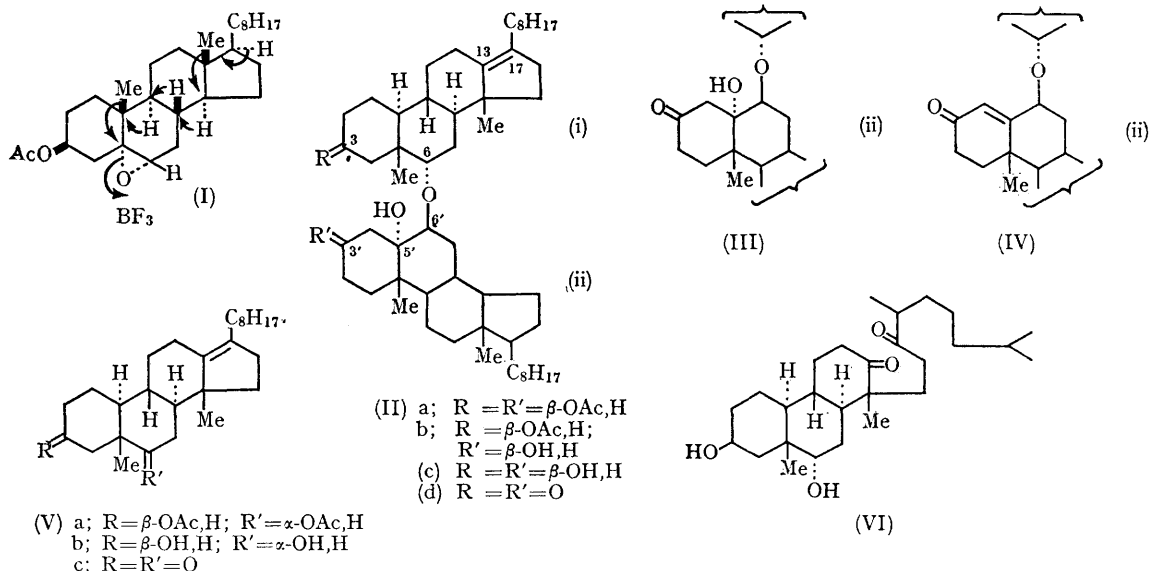
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BRIEF reaction of a concentrated solution of 3 $\beta$ -acetoxy-5,6 $\alpha$ -epoxy-5 $\alpha$ -cholestane (I) in benzene with boron trifluoride etherate gave the ether (IIa) (32% yield). A molecular-weight determination (804; Rast) and analysis showed the ether (IIa) to be dimeric, of molecular formula  $C_{58}H_{96}O_6$  (888). The presence of two acetate groups and only one tertiary alcohol function were indicated by infrared and n.m.r. spectra (60 Mc/sec.) and an active-hydrogen determination. The remaining oxygen atom was assigned as a di-secondary ether bridge between the steroid nuclei from the presence of two 1-proton peaks (6 $\beta$ -H, 2.95 p.p.m.; 6' $\alpha$ -H, 3.12 p.p.m.) in the n.m.r. spectrum. Finally, the presence in (IIa) of a tetrasubstituted double bond, exocyclic to at least one ring, was indicated by the ultraviolet spectrum ( $\epsilon_{2070}$  9,000;  $\epsilon_{2100}$  7,400;  $\epsilon_{2150}$  4,300;  $\epsilon_{2200}$  1,500) and the absence of signals due to vinylic protons in the n.m.r. spectrum.

(III) ( $a + 48$ ) was consistent with a 3-oxo-5 $\alpha$ -steroid. Dehydration of the hydroxy-ketone (III) yielded the 3'-oxo-4'-ene-6' $\beta$ -ether system (IV), confirmed by infrared (1672  $\text{cm}^{-1}$ ), ultraviolet ( $\epsilon_{2360}$  19,500), and n.m.r. spectra (6 $\beta$ -H, 2.97 p.p.m.; 6' $\alpha$ -H, 3.83 p.p.m.; 4'-H, 5.60 p.p.m.).

Treatment of ether (IIa) with lithium aluminium hydride gave the triol (IIc) which on mild oxidation yielded the 5' $\alpha$ -hydroxy-3,3'-diketone (IId). Substitution of the hydroxy-ketone (III) Cotton curve from that for (IId) gave a curve ( $a - 53$ ) consistent with a 3-oxo-5 $\beta$ -methyl-10 $\alpha$ -structure for nucleus (i).

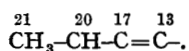
Reaction of the keto-ether (IV) with hydrogen bromide-acetic anhydride gave essentially two compounds in similar yields identified as cholesta-4,6-dien-3-one and the  $\Delta^{13(17)}$ -3 $\beta$ ,6 $\alpha$ -diacetate (Va) by infrared, ultraviolet, and n.m.r. spectra. In the n.m.r. spectra of the diacetate (Va), the diol



The nature of rings A and B in nucleus (ii) was deduced as follows. Alkaline hydrolysis of (IIa) gave the 3 $\beta$ -acetoxy-3' $\beta$ ,5' $\alpha$ -diol (IIb) which on mild oxidation gave the 3 $\beta$ -acetoxy-5' $\alpha$ -hydroxy-3'-ketone (III). The Cotton curve for the ketone

(Vb) derived from it by brief treatment with lithium aluminium hydride, and the diketone (Vc) the 21- $\text{CH}_3$  protons appeared as a doublet (1.00 and 0.90 p.p.m.) which could be reduced to a singlet by a decoupling frequency of  $-90$  c./sec. The

hydrogen atom at C-20 shows a peak at 2.45 p.p.m. These data are consistent with a partial structure



The location of the double bond at 13(17) was confirmed by spectral data on the ozonolysis product (VI) of diol (Vb). The infrared spectrum [ $\nu_{\text{max}}$  (CCl<sub>4</sub>) 1710 cm.<sup>-1</sup>] and the presence of signals in the n.m.r. spectrum assigned to the 21-CH<sub>3</sub> group (1.12 and 1.00 p.p.m.) which reduced to a singlet on irradiation with a frequency -88 c./sec. support structure (VI) for the ozonolysis product.

The ether (IIa) is considered to be formed by

nucleophilic attack by the epoxide oxygen of one epoxide molecule (i) to give normal diaxial opening of a 5 $\alpha$ ,6 $\alpha$ -epoxide in molecule (ii). The C-5-O cleavage in molecule (i) is accompanied by a sequence of 1,2-shifts as in (I) culminating with the loss of the hydrogen atom from C-17, to form the 13(17)-double bond and resulting in inversion at each ring junction.

Further steroidal systems are being studied in order to determine the factors which favour this "back-bone" rearrangement.

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