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REACTION OF EPOXIDES—XI*

A NOVEL "BACKBONE REARRANGEMENT" OF THE CHOLESTANE SKELETON

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Abstract—Purified BF_3-etherate reacts with 3β-acetoxy-5,6α-epoxy-5α-cholestane(I) at high concentrations in benzene to give the unsymmetrical di-steroidal ether (IIa). The formation of the ether (IIa) involves a novel "backbone rearrangement" of one of the steroidal skeletons, giving the 5β,14β-dimethyl 18,19-bisnor structure with all ring junction configurations inverted. 3,3-Ethylene dioxy-5,6β-epoxy-5β-cholestane reacts with BF_3-etherate to give the rearranged monomeric product (IVd), among other products. 3β,5,6β-Triacetoxy-5α-cholestane undergoes a similar "backbone" shift on treatment with BF_3-etherate in acetic anhydride at 80°.

IN THE course of our studies[1] of the behaviour of steroidal epoxides when treated with BF_3-etherate a variety of hydroxy-olefins was obtained in addition to aldehydes, ketones and vicinal fluorohydrins. These hydroxy-olefins, the structures of most of which remain unknown, were isolated in yields ranging from 10–90%. At no time in our studies was it possible to relate the occurrence of these hydroxy-olefins to any structural feature of the reacted epoxides. The mere identification of these hydroxy-olefins presented major problems as the available data indicated that they were products of skeletal rearrangements, rather than of simple elimination reactions. We therefore determined to examine the reactions of relatively accessible epoxides with BF_3-etherate as an initial step towards an understanding of the mode of formation of hydroxy-olefins.

Henbest *et al.*[2] examined the reaction of the 3β-acetoxy-5α,6α-epoxide (I) with BF_3-etherate and reported the isolation of the 5α-hydroxy-6β-fluoro derivative as the major product, accompanied by starting material and a polar fraction which was not examined further. Accordingly we proposed to examine this polar fraction (presumably alcohol(s)) derived as it was from the readily accessible 5α,6α-epoxide (I). Reaction of a 5% solution of the steroid in benzene with BF_3-etherate gave, after chromatography, in addition to fluorohydrin and starting material, a further crystalline material (10%) shown below to have structure IIa. The NMR spectrum of IIa suggested either a molecular compound (1:1) or an unsymmetrical dimer, the latter being supported by a molecular weight determination (Rast, 804; dimer requires ca. 888). Subsequently a higher yield (32%) of the dimer was obtained by performing the reaction at the highest possible steroid concentration. The BF_3-etherate was purified by repeated redistillation to free it from HBF_4. The formation of fluorohydrin

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[*] Part X. J. W. Blunt, M. P. Hartshorn and D. N. Kirk, *Chem. Comm.* 160 (1966).

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[1] J. W. Blunt, M. P. Hartshorn and D. N. Kirk, *Tetrahedron* **22**, 1421 (1966); M. P. Hartshorn and D. N. Kirk, *Tetrahedron* **21**, 1547 (1965) and Refs. cited therein.

[2] H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.* 4765 (1957).

was then suppressed, in accordance with the reported[3] influence of HBF_4 concentration (as added HF) on the yield of fluorohydrin. We consider that BF_3-etherate freed from HBF_4 must be used in order that the BF_3 may exert its full effect as a Lewis acid, uncomplicated by the presence of nucleophilic fluorine containing species.

The structure IIa of the dimer rests upon the following evidence. The elemental analysis, assuming no change of oxidation level, was consistent with a molecular formula $C_{58}H_{96}O_6$. Of the six oxygen atoms present, four were accounted for as two acetate groups (NMR data) and one oxygen atom as a tertiary alcohol (active hydrogen determination, IR and NMR spectra). The tertiary nature of the hydroxyl group was confirmed by its failure to undergo acetylation or oxidation under normal conditions. The remaining oxygen atom was assigned to an ether function, the most attractive placing of which was as a bridge between the two steroid nuclei. Furthermore, the NMR spectrum of IIa exhibited two one-proton signals (2·97 and 3·13 ppm*) consistent with an ether bridge between two secondary carbon atoms.

The presence of a double bond, tetrasubstituted (NMR) and probably exocyclic to at least one ring, was inferred from the UV spectrum of IIa in the 2200–2070 Å region (ε_{2070} 9000). The double bond, which was not reduced by hydrogen–platinum in acetic acid containing perchloric acid or isomerized by hydrogen chloride in chloroform, gave a positive test with tetranitromethane.

The NMR spectrum of IIa exhibited a single three-proton peak at 0·67 ppm assigned to the C-18 methyl group of a cholestane derivative the functional groups of which were well removed from C-18. The absence of further signals below 0·80 ppm suggested that only one steroid nucleus of the dimer had a normal unsubstituted and saturated structure in rings C and D. The other steroid nucleus had clearly been altered in the C/D ring system, probably by the presence of a double bond resulting in the shift of the C-18 resonance for this nucleus to lower field. Evidence detailed below indicates the rearranged 14β-methyl-$\Delta^{13(17)}$-structure for this part of the dimer molecule.

Hydrolysis of IIa with aqueous methanolic potassium hydroxide gave only the dihydroxy-monoacetate (IIb). The second acetoxy group, known to be of secondary type (NMR data), was resistant to hydrolysis in accordance with its hindered axial conformation. Its removal was achieved by treatment of (IIa) with lithium aluminium hydride to give the triol (IIc). Oxidation of the dihydroxy-monoacetate (IIb) with chromic acid in acetone gave the hydroxy-keto-acetate (IId), the Cotton curve (a +48) for which is consistent with the assignment of IId as a 5α-cholestan-3-one derivative.[4] Dehydration of (IId) with thionyl chloride–pyridine at 90° gave a conjugated ketone. The spectral data for this conjugated ketone allowed the partial structure (III) to be deduced and assigned tentatively to the normal steroid nucleus (see above). The Δ^4-3-keto-system was supported by the IR (1672 cm^{-1}), UV (λ_{max} 2360 Å; ε, 19,500) and NMR spectra ($C^{4'}$–H; 5·60 ppm). The location and stereochemistry of the ether bridge in partial structure (III) (and hence in the normal nucleus (ii) of the dimer) also followed from spectroscopic data. The allylic position of the ether bridge was supported by the further chemical shift (from 3·12 ppm to

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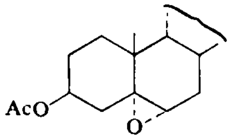
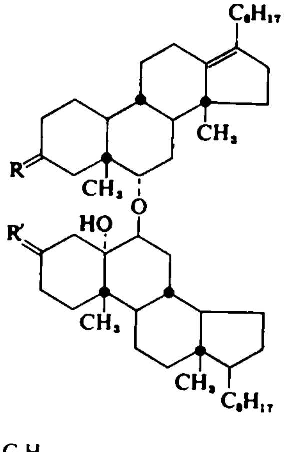
* NMR spectra determined at 60 Mc for CCl_4 solutions are quoted as chemical shifts from TMS as internal standard.

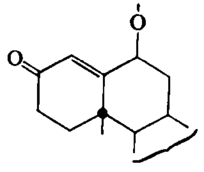
[3] A. Bowers and H. J. Ringold, U.S.P at. 3115492; *Chem. Abstr.* **61**, 3179g (1964).

[4] C. Djerassi, *Optical Rotatory Dispersion* McGraw-Hill, New York (1960).



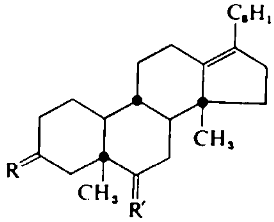
I



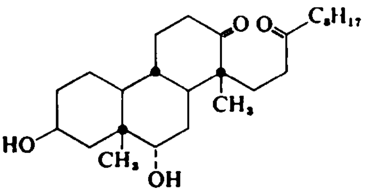


III

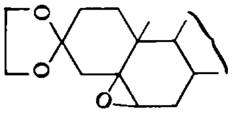
II a R,R'; βOAc, H.
b R; βOAc, H; R'; βOH, H.
c R, R'; βOH, H.
d R; βOAc; H: R'; O.
e R, R'; O.
f R; O: R'; βOAc, H.



IV a R; βOAc, H: R'; αOAc, H.
b R; βOH, H: R'; αOH, H.
c R, R'; O.
d R; O; R'; βOH, H.
e R, R'; βOAc, H.
f R, R'; βOH, H.



V



VI

3·83 ppm) of the 6'α-H signal in the NMR spectrum as a result of introducing the $\Delta^{4'}$-double bond. Furthermore the UV spectrum (λ_{max} 2360 Å) is consistent with a Δ^4-3-keto-6β-oxygen system but not with the 6α-epimer which might be expected[5] to give a UV peak at ca. 2400 Å.

Oxidation of the triol (IIc) gave the diketone (IIe). On the reasonable assumption that the observed Cotton effect (a −16) of the diketone (IIe) would be the resultant of the superimposed curves for the separate ketone functions, the Cotton effect of the 3-monoketone (IIf) was estimated by a graphical subtraction of the Cotton curve for (IId) from that of the diketone (IIe). A new curve of amplitude a −53 was obtained consistent with the 3-keto-5β-methyl-10α-H formulation of (IIf). The implied assignment of the partial structure 3β-acetoxy-5β-methyl-10α-H to nucleus (i) of the dimer molecule is supported by the observed resistance of the sterically-hindered and axial 3β-acetoxy group to hydrolysis.

Treatment of the conjugated ketone (III) with hydrogen bromide–acetic anhydride gave as major products in approximately equal quantities a diacetate (IVa) and cholesta-4,6-dien-3-one. The isolation of cholestadienone from the cleavage reaction is clear evidence in support of the assignment of functional group positions and of the normality of steroid nucleus (ii). Reaction of the diacetate (IVa) with lithium aluminium hydride gave the diol (IVb) which was oxidized by chromic acid in acetone

[5] L. Dorfman, *Chem. Revs.* 53, 47 (1953).

to the corresponding diketone (IVc). The assignments of signals exhibited in the NMR spectra of these and other related compounds are given in Table 1.

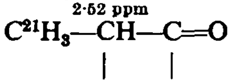
Ozonolysis of the diol (IVb) gave a D-seco-diketone (V) the IR spectrum (1711 cm^{-1}) of which is consistent with the presence of acyclic and/or six-membered ring ketones but excluded any structure including a five-membered ring ketone. The NMR spectrum of the D-seco-diketone (V) exhibited signals at 1·11 and 1·00 ppm assigned to the 21-methyl group split by the adjacent proton at C-20. Double irradiation with a frequency of −88 c/s reduced the 21-methyl doublet to a singlet. These data are consistent with the partial structure  $C^{21}H_3—\overset{2\cdot52\ \mathrm{ppm}}{\underset{|}{C}H}—\underset{|}{C}=O$ for the diketone (V), and the consequent assignment of the double bond in diacetate (IVa) to the 13,17-position. The above assignment of signals in the NMR spectrum of diketone (V) was confirmed by examination of the NMR spectrum of a model compound, isopropyl methyl ketone. A six proton doublet at 1·12 and 1·00 ppm assigned to the *gem*-dimethyl protons was reduced to a singlet on double irradiation with a frequency of −88 c/s. The methine proton in isopropyl methyl ketone was assigned to a one-proton multiplet at 2·52 ppm in excellent agreement with the data for the D-seco-diketone (V).

Table 1. NMR data (in ppm) for $\Delta^{13(17)}$-derivatives

Comp	14β-CH_3	3-H	6-H	5β-CH_3 found	5β-CH_3 calc.
IVa	0·90	5·05 (7)	4·57 (5)	1·08	1·08
IVe	0·90	4·97 (6)	4·47 (12)	1·02	1·00
IVb	0·90	4·20 (7)	3·40 (8)	1·15	1·11
IVf	0·91	4·17 (6)	3·25 (12)	1·08	1·05
IVc	0·98	—	—	1·05	1·08
IVd	0·90	—	3·33 (14)	0·78	0·78
V	1·18	4·23 (7)	3·47 (8)	1·08	1·11

* Figure in parentheses gives width at half-height in c/s.

Confirmatory double irradiation experiments were subsequently carried out on the diol (IVb) and the diketone (IVc), the super-imposed frequencies required to reduce the 21-methyl doublet (1·00 and 0·90 ppm) to a singlet being −90 c/s and −87 c/s respectively. From this data the methine proton at C-20 in the diol (IVb) and the diketone (IVc) could be located at 2·45 ppm and 2·40 ppm respectively. For a similar compound $(CH_3)_2—CH—CH=CH—CH_3$, the *gem*-dimethyl protons can be assigned to a six-proton doublet at 1·00 ppm and 0·90 ppm and the adjacent methine proton to a one-proton signal centred at 2·50 ppm.

The ether (IIa) is considered to be formed from the 5α,6α-epoxide (I) by nucleophilic attack by the epoxide oxygen atom of one epoxide molecule (i) to give normal diaxial opening of the 5α,6α-epoxide linkage in molecule (ii). The epoxide ring of molecule (i) must undergo C_5—O bond cleavage followed by a sequence of *cis*-1,2-shifts, beginning with the migration of the 10β-methyl group to the 5β-position and ending with migration of the 13β-methyl group to the 14β-position and loss of the 17α-proton to form the 13,17-double bond. This backbone rearrangement, which closely resembles known rearrangements[6] in the pentacyclic triterpene group, involves inversion at each of the ring junctions.

During our earlier study[1] of the reaction of 3,3-ethylene-dioxy-5,6β-epoxy-5β-cholestane (VI) with BF_3 a minor product (10%) was isolated to which the rearranged structure (IVd) is now assigned. The structure of the hydroxy-ketone (IVd) was supported by its IR (3570 and 1710 cm^{-1}) and UV spectra (ε_{2050} 9600). Oxidation of the hydroxy-ketone (IVd) gave a product identical in all respects with the diketone (IVc) obtained from the ether (IIa). The Cotton curve (*a* −66) for the hydroxy-ketone (IVd) is consistent with a 3-keto-5β-methyl-10α-H structure and is in good agreement with the amplitude (*a* −53) calculated above for the 3-monoketone (IIf) in the dimeric series.

It is uncertain whether the hydroxy-ketone (IVd) represents a product of reaction of BF_3-etherate with the 3,3-ethylenedioxy-compound (VI) or the corresponding 3-ketone. However, it is clear that the C_5—O bond cleavage can not be concerted with the migration of the 19-methyl group to the β-face of C-5. It is probable that the sequence of 1,2-shifts comprising the backbone rearrangement originate in the formation of a discrete C-5 carbonium ion.

The diacetate (IVe), the major product of the reaction of 3β,5,6β-triacetoxy-5α-cholestane with BF_3-etherate in acetic anhydride originally reported[7] by Snatzke and Fehlhaber, has recently been shown[8] to have a 18,19-bisnor-5β,14β-dimethyl structure in which the skeleton has undergone a backbone rearrangement. The structure was established by NMR spectra and conversion into the diketone (IVc) reported above.

NMR *spectra*

The calculated values for the 5β-methyl resonance frequency (see Table 1) were estimated on the basis of a 5β-methyl resonance frequency of 0·85 ppm for the unsubstituted backbone rearranged skeleton and additivity values of the chemical shift for substituents as shown in Table 2. These additivity values were derived by assuming that the effects of 6α-OH, 6α-OAc, 3-ketone, 3β-OH, 3β-OAc substituents on the 5β-methyl resonance in a 5β,10α-structure (IV) would be equivalent to the effects of 1α-OH, 1α-OAc, 2-ketone, 2β-OH, 2β-OAc substituents respectively on the 19-CH_3 resonance of a 5α-cholestane compound.[9] The value of −0·05 ppm for the 6β-OH substituent was derived by analogy with the effect of a 17aβ-OH substituent on the 18-CH_3 resonance in a D-homosteroid.[10] The value of +0·25 ppm for the 6-ketone substituent was estimated from the effect of 4- and 6-ketone substituents on the 5α-methyl resonance frequency for 5-methyl-5α-cholestane derivatives. The apparent analogy between the probable effect of 6β-OH and 6-ketone substituents for the backbone rearranged skeleton 5β-CH_3 resonance and the effect of 1β-OH and 1-ketone substituents on the 19-CH_3 resonance for a 5α-cholestane derivative was rejected because of the probable distortion of ring A in

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[6] J. L. Courtney, R. M. Gascoigne and A. Z. Szumer, *J. Chem. Soc.* 881 (1958), and Refs. cited therein.

[7] G. Snatzke and H. Fehlhaber. *Liebig's Ann.* **676**, 188 (1964).

[8] J. W. Blunt, M. P. Hartshorn and D. N. Kirk, *Tetrahedron Letters* No. 19, 2175 (1966).

[9] R. F. Zurcher, *Helv. Chimica Acta* **46**, 2054 (1963),

[10] N. R. Trenner, B. H. Arison, D. Taub and N. L. Wender, *Proc. Chem. Soc.* 214 (1961).

TABLE 2. ADDITIVITY VALUES FOR 5β-METHYL RESONANCE IN BACKBONE REARRANGED SKELETON (IV)

Substituent	Increment (ppm) of chemical shift
6α-OH	+0·01
6α-OAc	+0·08
6β-OH	−0·05
6β-OAc	0·00
6-ketone	+0·25
3-ketone	−0·02
3β-OH	+0·25
3β-OAc	+0·15

these compounds due to non-bonded interactions between the 1-substituent and the 11β-hydrogen atom.

The configurations assigned above to the 3- and 6-acetoxy and hydroxy groups in the backbone rearranged steroids are confirmed by the half-band width data (see Table 1) for the geminal proton resonances. Equatorial protons at C-3 or C-6 exhibit signals with half-band widths in the range 5–8 c/s whereas the axial protons exhibit signals with half-band widths in the range 12–14 c/s.[11]

EXPERIMENTAL

Rotations $CHCl_3$ solns. at room temp. IR spectra (Perkin–Elmer 221 or 137 spectrometer). UV spectra (EtOH). Alumina used for chromatography was P. Spence, Grade H, deactivated by the addition of 5% of 10% AcOH. Light pet. refers to the fraction of b.p. 50–70°. ORD curves were kindly determined at Westfield College, London, by courtesy of Prof. W. Klyne. UV Spectra in the 200–220 mμ region (EtOH sols.[12] in a 1 mm cell; Beckmann DK2A spectrometer).

Reaction of 3β-Acetoxy-5,6α-epoxy-5α-cholestane with BF_3*-etherate.* Redistilled BF_3-etherate (24 ml) was added to a soln. of the steroid (24 g) in dry benzene (30 ml) and kept at 20° for 45 sec. The reaction was quenched by pouring the mixture into excess of dry ether followed by treatment with saturated $NaHCO_3$ aq. Crystallization from ether of the crude product, isolated by means of ether, gave the *dimeric ether* (IIa; 6·4 g) as prisms, m.p. 181–183°, $[\alpha]_D$ +10° (*c* 1·00), ν_{max} (CS_2) 1740, 1242 (OAc), 3460 cm^{-1} (OH), λ 207 mμ (ε 9000), 210 mμ (ε 7400), 215 mμ (ε 4300), 220 mμ (ε 1500). (Found: C, 78·55; H, 11·2. M.W., 804 (Rast) $C_{58}H_{96}O_6$ requires C, 78·4; H, 10·8%. M.W., 888). NMR ($CDCl_3$) 3α-H, 5·15; 6β-H, 2·97; 5β-CH_3, 1·01; 14β-CH_3, 0·91; $C^{21}H_3$, 1·01 and 0·91; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·90; 3′α-H, 5·15; 6′α-H, 3·13; $C^{18'}H_3$, 0·67; $C^{19'}H_3$, 1·15; $C^{21'}H_3$, $C^{26'}H_3$, $C^{27'}H_3$, 0·81 and 0·90; OAc (6 proton), 2·05 ppm. The residue from the crystallization was adsorbed on to alumina (750 g). Elution with light pet.–benzene gave a gum (4·1 g). Further elution with the same solvent gave 3β-acetoxy-6β-fluoro-cholestan-5α-ol (4·0 g), which crystallized from EtOH to give m.p. 210–212°. Finally, elution with benzene gave a gum (9 g) from which further IIa (1·2 g) was obtained by crystallization.

Triol (IIc). A sol. of the ether (IIa; 3·78 g) in ether (150 ml) was treated with LAH (2 g) at 35° for 45 min. Isolation by means of CH_2Cl_2 gave the triol as an amorphous solid (2·3 g), m.p. 233–237°, $[\alpha]_D$ +19° (*c* 0·68), ν_{max} (nujol) 3390 cm^{-1}, NMR ($CDCl_3$) 3α-H, 4·20; 6β-H, 2·93; 5β-CH_3, 1·00; 14β-CH_3, 0·91; $C^{21}H_3$, 1·00 and 0·90; $C^{26}H_3$, $C^{27}H_3$, 0·90 and 0·80; 3′α-H, 4·17; 6′α-H, 3·15; $C^{18'}H_3$, 0·67; $C^{19'}H_3$, 1·11; $C^{21'}H_3$, $C^{26'}H_3$, $C^{27'}H_3$, 0·90; and 0·82 ppm.

Oxidation of a sample of the troil with pyridine–CrO_3 complex gave the diketone (IIe) as a gum $[\alpha]_D$ 0° (*c* 0·92), ν_{max} (film) 3390 cm^{-1} (OH) and 1715 cm^{-1} (C=O). ORD (Dioxan) a^{315}_{280} −16.

Dihydroxyacetate (IIb). A soln. of the ether (IIa; 9·4 g) and KOH (6 g) in MeOH (600 ml) was

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[11] N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, Holden-Day (1964).

[12] O. H. Wheeler and J. L. Mateos, *J. Org. Chem.* **21**, 1110 (1956).

heated under reflux for 15 min. The solid which separated when the soln was cooled crystallized from acetone to give the *dihydroxyacetate* (IIb) as needles (8·6 g), m.p. 136–137°, $[\alpha]_D$ +26° (*c* 1·09), ν_{max} (nujol) 3390 cm^{-1} (OH), 1736 and 1250 cm^{-1} (OAc). (Found: C, 80·0; H, 11·3. $C_{56}H_{94}O_5$ requires: C, 79·5; H, 11·1%.) NMR ($CDCl_3$) 3α-H, 5·11; 6β-H, 2·93; 5β-CH_3, 0·99; 14β-CH_3 0·91; $C^{21}H_3$, 0·98 and 0·88; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·88; 3′α-H, 4·00; 6′α-H, 3·13; $C^{18\prime}H_3$, 0·67; $C^{19\prime}H_3$, 1·15; $C^{21\prime}H_3$, $C^{26\prime}H_3$, $C^{27\prime}H_3$, 0·81 and 0·90; OAc (3-protons), 2·01 ppm.

Hydroxy-keto-acetate (IId). A soln of IIb (8·5 g) in acetone (300 ml) at 0° was treated with 8N CrO_3 soln. Isolation of the product by means of pentane and recrystallization from acetone gave IId as needles (6·3 g), m.p. 209–210°, $[\alpha]_D$ +34° (*c* 1·0), ν_{max} (CS_2) 3390 (OH), 1733 and 1235 (OAc) and 1710 cm^{-1} (C═O). (Found: C, 80·1; H, 11·3. $C_{56}H_{92}O_6$ requires C, 79·6; H, 10·9%.) ORD (Dioxan) a^{305}_{266} +48. NMR ($CDCl_3$) 3α-H, 5·10; 6β-H, 2·95; 5β-CH_3, 1·00; 14β-CH_3, 0·90; $C^{21}H_3$, 0·90 and 1·00; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·88; 6′α-H, 3·11; $C^{18\prime}H_3$, 0·68; $C^{19\prime}H_3$, 1·31; $C^{21\prime}H_3$, $C^{26\prime}H_3$, $C^{27\prime}H_3$, 0·81 and 0·90; OAc (3-protons), 2·00 ppm.

Keto-acetate (III). A soln of IId (1 g) and $SOCl_2$ (0·24 ml) in pyridine (20 ml) was kept at 90° for 15 min. The crude product, isolated by means of pentane–ether, was filtered through alumina. Elution of the column with benzene gave the *keto-acetate* (III) which crystallized from MeOH–ether as needles (610 mg), m.p. 191–191·5°, $[\alpha]_D$ +37° (*c* 1·0), ν_{max} (CS_2) 1730 and 1238 (OAc), 1672 cm^{-1} (C═C—C═O), λ_{max} 236 mμ (ε 19500). (Found: C, 81·3; H, 11·2. $C_{56}H_{90}O_4$ requires: C, 81·4; H, 10·9%.) NMR (CCl_4) 3α-H, 5·01; 6β-H, 2·97; 5β-CH_3, 1·00; 14β-CH_3, 0·91; $C^{21}H_3$, 0·90 and 1·00; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·90; 4′-H, 5·60; 6′α-H, 3·83; $C^{18\prime}$-H_3, 0·70; $C^{19\prime}H_3$, 1·25; $C^{21\prime}H_3$, $C^{26\prime}H_3$, $C^{27\prime}H_3$ 0·81 and 0·90; OAc (3-protons), 1·93 ppm.

Cleavage of Keto-acetate (III). A soln of the steroid (2·35 g) in CCl_4 (15 ml) and Ac_2O (50 ml) was treated with HBr aq (60%; 3 ml) in Ac_2O (25 ml) and the soln kept at 20° for 18 hr. The crude product, isolated by means of ether was adsorbed on to alumina (200 g). Elution with light pet.–benzene (19:1) gave gums (328 mg) shown to be a mixture (TLC). Careful elution with light pet.–benzene (3:1 and 2:1) gave a series of fractions (total 1·5 g). TLC evidence suggested the presence of roughly equal amounts of two compds, the earlier fractions consisting largely of cholesta-4,6-dien-3-one and the later fractions of the diacetate (IVa). An early fraction gave ν_{max} (film) 1664, 1613, 1582 cm^{-1} (C═C—C═C—C═O), λ_{max} 285 mμ, NMR (CCl_4) 4-H, 6-H, 7-H, 6·01 and 5·51; $C^{18}H_3$, 0·75; $C^{19}H_3$, 1·10; $C^{21}H_3$, $C^{26}H_3$, $C^{27}H_3$, 0·81 and 0·90 ppm. Reaction with 2,4-dinitrophenylhydrazine gave a dark red derivative, m.p. 227–228°, lit. value[18] m.p. 231–232°.

Later fractions gave slightly impure (cholestadienone) diacetate (IVa), ν_{max} (film) 1730, 1240 cm^{-1} (OAc), NMR (CCl_4), 3α-H, 5·05; 6β-H, 4·57; 5β-CH_3, 1·08; 14β-CH_3, 0·90; $C^{21}H_3$, 1·02 and 0·92 $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·89; OAc (total 6 protons), 2·00 and 1·95 ppm.

Finally benzene eluted starting material (400 mg), m.p. 190–191°.

Diol. (IVb) Treatment of the crude diacetate (IVa) with LAH (excess) in ether at 35° for 30 min gave a crude product which was adsorbed on to alumina. Elution with benzene–ether (9:1) gave the *amorphous diol*, $[\alpha]_D$ +37° (*c* 0·65), pure by TLC, ν_{max} (CS_2) 3559 cm^{-1} (OH). (Found: C, 80·1; H, 11·5; $C_{27}H_{46}O_2$ requires: C, 80·6; H, 11·4%.) NMR ($CDCl_3$) 3α-H, 4·20; 6β-H, 3·40; 5β-CH_3, 1·15; 14β-CH_3, 0·90; $C^{21}H_3$, 1·00 and 0·90; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·90 ppm. Double irradiation with −90 c/s collapsed $C^{21}H_3$ doublet to a singlet.

Ozonolysis of diol (IVb). The diol (IVb; 80 mg) in $CHCl_3$ at −10° was reacted with a stream of ozonized oxygen for 45 min. The crude product, on removal of the $CHCl_3$ was treated with Zn dust (100 mg) and AcOH (10 ml) at 20° for 2 hr. Isolation by means of ether gave the slightly impure D-seco-diketone (V), ν_{max} (CS_2) 3350 (OH). 1711 cm^{-1} (C═O), NMR ($CDCl_3$) 3α-H, 4·23; 6β-H, 3·47; 5β-CH_3 and 14β-CH_3, 1·08 and 1·18; $C^{21}H_3$, 1·00 and 1·11; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·89 ppm. Double irradiation with −88 c/s collapsed the $C^{21}H_3$ doublet to a singlet.

Oxidation of Diol (IVb). Oxidation of (IVb) with 8N CrO_3 soln in acetone gave the diketone (IVc) as a gum (pure by TLC), $[\alpha]_D$ +34° (*c* 0.79), ν_{max} (film) 1720 and 1710 cm^{-1} (C═O), NMR (CCl_4) 5β-CH_3, 1·05; 14β-CH_3, 0·98; $C^{21}H_3$, 1·00 and 0·90; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·90 ppm. Double irradiation with −87 c/s collapsed the $C^{21}H_3$ doublet to a singlet.

Oxidation of Hydroxy-ketone (IVd). The hydroxy-ketone (IVd), m.p. 124–126°, $[\alpha]_D$ −6° (*c* 1·05), ν_{max} (CS_2) 3570 (OH), 1710 cm^{-1} (C═O), (Found: C. 81·25; H, 11·3. $C_{27}H_{44}O_2$ requires C, 81·0; H, 11·0%.) ORD a^{303}_{265} (MeOH) −66, NMR (CCl_4) 6 α-H, 3·33 (multiplet); 5β-CH_3, 0·78; 14β-CH_3, 0·90; $C^{21}H_3$, 1·02 and 0·92; $C^{26}H_3$, $C^{27}H_3$, 0·80 and 0·90 ppm, was oxidized by 8N CrO_3

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[18] V. Petrow, *J. Chem. Soc.* 66 (1940).

soln in acetone to give a diketone identical in all respects with diketone (IVc) derived from ether (IIa).

Diol (IVf). Reaction of the diacetate (IVe), λ 200 mμ (ε 13000), 205 mμ (ε 11200), 210 mμ (ε 8300), 215 mμ (ε 5300), 220 mμ (ε 2660), NMR (CCl_4) 3α-H, 4·97; 6α-H, 4·47; 5β-CH_3, 1·02; 14β-CH_3, 0·90; $C^{21}H_3$, 0·90 and 1·00; $C^{26}H_3$, $C^{27}H_3$, 0·79 and 0·89 ppm; OAc (6 protons), 1·97 ppm prepared by treatment[7] of 3β,5, 6β-triacetoxy-5α-cholestane with BF_3–Ac_2O at 80°, with LAH (excess) in ether at 35° for 30 min. gave the diol (IVf), m.p. 190–191·5°,]α]$_D$ +18° (*c* 1·00) (lit. values,[7] m.p. 192–193°, [α]$_D$ +21°), NMR ($CDCl_3$) 3α-H, 4·17; 6α-H, 3·25; 5β-CH_3, 1·08; 14β-CH_3, 0·91; $C^{21}H_3$, 0·90 and 1·00; $C^{27}H_3$, $C^{27}H_3$, 0·79 and 0·89 ppm. Double irradiation with −88 c/s collapsed the $C^{21}H_3$ doublet to a singlet.

Oxidation of Diol (IVf). Oxidation of the diol (IVf) with 8N CrO_3 soln in acetone gave a gum, [α]$_D$ +33 (*c* 0·99), IR and NMR spectra identical with those for diketone (IVc) obtained earlier.

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