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REACTIONS OF EPOXIDES—IX*

THE BORON TRIFLUORIDE CATALYSED REARRANGEMENT OF SOME 3,3-ETHYLENEDIOXY-5,6-EPOXYCHOLESTANES

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Abstract—The 3,3-ethylenedioxy-6α-methyl-5β,6β-epoxide (I) undergoes a novel ring A cleavage reaction with boron trifluoride. The 5α,6α-epoxide (IV) gives the expected A-homo-B-nor-4a-ketone, which undergoes further reactions involving the ketal group. The 6α-hydrogen-5β,6β-epoxide (XIIIa) rearranges to give mainly 5α-6-ketonic products, together with 6% of the A-seco-diene (XV). Mechanisms are suggested for these various reactions.

BORON trifluoride catalysed rearrangements of derivatives of 5α,6α-epoxides with or without the presence of a 6-methyl group have been described.[1–3] In the 6β-hydrogen series, both 3-deoxy- and 3α-acetoxy- derivatives rearrange to 5β-6-ketones in low yield. In contrast the 3β-acetoxy-, 3-keto- and 3,3-ethylenedioxy- derivatives, not having an energetically favourable conformational change in assuming the 5β-configuration, and having the C_5–O epoxide bond stabilized by the –I effect of the C-3 substituent, exhibit C_6–O cleavage with the formation of the 5α-hydroxy-6β-fluoro- derivatives.

5β,6β-Epoxycholestanes bearing 3β-substituents suffer initial attack by fluoride ion at C-5[1,3] although, as we have shown,[3] the resulting fluorohydrins may react further with boron trifluoride. Since a 3,3-ethylenedioxy substituent should sterically hinder attack of fluoride ion at C–5 and also, by virtue of its –I effect, inhibit 6-ketone formation we decided to examine the behaviour of the 3,3-ethylenedioxy-5β,6β-epoxides, with and without a 6α-methyl substituent, towards boron trifluoride. The reaction of 3,3-ethylenedioxy-5α,6α-epoxy-6β-methylcholestane was also examined, although it could be predicted that the preferred reaction with boron trifluoride would be the normal C_6–O cleavage with rearrangement to give the A-homo-B-nor-4a-ketone.[3]

6-Methyl epoxides

The 3,3-ethylenedioxy-6-methyl-5,6-epoxycholestanes were obtained by the epoxidation of 3,3-ethylenedioxy-6-methylcholest-5-ene resulting from the ketalization of 6-methylcholestenone. The configurations of the epoxides (formed in equal amounts) were assigned by comparison of molecular rotation difference data for the epoxides with those for the corresponding 3β-acetoxy-6-methyl-5,6-epoxy- and 3,3-ethylenedioxy-5,6-epoxy-cholestanes.

* Part VIII, J. W. Blunt, M. P. Hartshorn and D. N. Kirk, *Chem. Comm.* 545 (1965).

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[1] H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.* 4596, 4765 (1957).
[2] A. Bowers, L. Ibanez and H. J. Ringold, *Tetrahedron* **7**, 138 (1959).
[3] J. W. Blunt, M. P. Hartshorn and D. N. Kirk, *Tetrahedron* **21**, 559 (1965).

Reaction of the 6α-methyl-5β,6β-epoxide (I) with boron trifluoride etherate in benzene solution was shown by TLC and specific rotation changes to be rapid (2 min). Chromatography on alumina allowed the separation of the major products. The first compound eluted was identified as 6-methylcholesta-4,6-dien-3-one (42%) by comparison with an authentic sample.

The second compound (44%) eluted was an oil to which the 2′-hydroxyethyl 3,4-seco-6-methylcholesta-4,6-dien-3-oate structure (IIa) was assigned on the following evidence. The diene structure was supported by the IR spectrum (1592 and 890 cm^{-1}) and the UV spectrum (λ_{max} 233 mμ (ε 20,500), 239 mμ (ε 23,000) and 246 mμ (ε 15,700)). In addition the NMR spectrum exhibited signals assigned as follows: C_7–H (τ 4·41), C_4-methylene protons (τ 5·01 and 4·93) and 6-methyl group (τ 8·17). The ester structure followed from the IR spectrum (3333, 1730 and 1176 cm^{-1}) and the NMR spectrum which exhibited the following signals: two two-proton multiplets centred at τ 6·13 and 5·77 assigned to the methylene groups of the 2′-hydroxyethyl portion; a two-proton broad signal at τ 7·78 assigned to the C_2-protons adjacent to the ester carbonyl group and split by the C_1-protons. The two-proton multiplets of the 2′-hydroxyethyl structure are assigned as $R—CO_2—\overset{\tau\ 5\cdot77}{CH_2}—\overset{6\cdot13}{CH_2}—OH$. This assignment and the structure of the ester were supported by NMR spectra of $CH_3(CH_2)_2—CO_2—\overset{\tau\ 5\cdot88}{CH_2}—\overset{6\cdot20}{CH_2}—OH$ (both multiplets) and

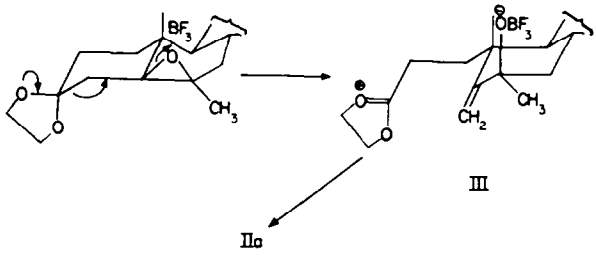
$$CH_3(CH_2)_2—CO_2—CH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$CH_3—CO_2—CH_2$$

(sharp four-proton singlet τ 5·80).

Reaction of the above diene-ester (IIa) with methanol containing a trace of concentrated hydrochloric acid for 7 hr at 20° achieved the partial exchange (38%) of methyl alcohol for ethylene glycol in the ester system. The methyl ester (IIb) exhibited identical IR, UV and NMR spectra with those of the 2′-hydroxyethyl ester except for features specifically associated with the alcohol component of the ester.

The mode of formation of 6-methylcholesta-4,6-dien-3-one in the reaction is not clear because the point at which the ketal group is lost can not be defined. However, it is pertinent to note that 6-methylcholesta-3,5-diene (40%) was formed[3] on treatment of 6α-methyl-5β,6β-epoxycholestane with boron trifluoride etherate in benzene solution.

It seems probable however, that the ketal group participates in the rearrangement leading to the diene-ester (IIa). The reaction is envisaged as proceeding by electron shifts as shown in Fig. 1 to give the intermediate (III) which on quenching with water would give rise to the observed product. Necessarily, as the ketal group is intimately



involved in the rearrangement, the reaction has no counterpart in the reactions of 3β-acetoxy or 3-deoxy-6α-methyl-5β,6β-epoxycholestanes.

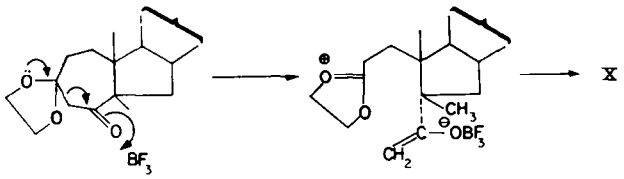
The reaction of the 3,3-ethylenedioxy-6β-methyl-5α,6α-epoxide (IV) with boron trifluoride proceeded with the expected skeletal rearrangement to a A-homo-B-nor-system but was complicated by transformations involving the ketal moiety. Brief reaction (3·5 min) in benzene solution gave a crude product which was shown (TLC) to contain at least five components. Chromatography on alumina allowed the separation of a fraction (43%) which was shown to consist of a mixture (ca. 7:4) of the A-homo-B-nor-3,3-ethylenedioxy-4a-ketone (V) and the A-home-B-nor-3, 4a-diketone (VI). The structure of the major component (V), separated partially from the mixture by crystallization, was deduced from IR and NMR spectra. The 5β-orientation was assigned by analogy with the corresponding 3β-acetoxy-compound.[4] The presence of the 3,4a-diketone (VI) in the mixture was deduced from the UV spectrum (λ_{max} 301 mμ)[4] of an ethanolic solution containing potassium hydroxide. The optical density of the solution allowed the relative proportions of the two compounds (V and VI) to be estimated. Hydrolysis of the mixture with aqueous acetic acid gave only the 3,4a-diketone (VI). Reaction of the 3,4a-diketone (VI) with pyridine-acetic anhydride gave an enol acetate[4] assigned the 3-acetoxy-Δ^3-4a-ketone structure (VII) on the basis of the IR and UV spectra and by comparison of the NMR spectra of the enol acetate with the ether (VIII) reported below (methyl signals at τ 8·77, 9·03, 9·10, 9·20 and 9·37 for VII compared with τ 8·83, 9·07, 9·10, 9·20 and 9·37 for the ether (VIII)).

Further elution with light petroleum–benzene mixtures gave ethane-1,2-diol di-(5-methyl-A-homo-B-nor-5β-cholest-3-en-4a-on-3-yl)-ether (IX; 23%). The dimeric nature of the ether was indicated by the mol. wt (Rast, Found; 780; calc. 854). The symmetry of the ether was supported by the simplicity of the NMR spectrum, the signals due to each steroid fragment being exactly superposed. The conjugated system in ring A followed from the IR and UV spectra (λ_{max} 255 mμ, ε 23,000 for M. W. 854), while the NMR spectrum exhibited signals for the C_4-olefinic protons (τ 4·78) and for the two-methylene bridging unit (τ 6·05). Hydrolysis of the ether (IX) with aqueous acetic acid again gave the 3,4a-diketone (VI).

A later fraction from the column was shown to be 2′-hydroxyethyl 5-methyl-A-homo-B-nor-5β-cholest-3-en-4a-on-3-yl ether (VIII; 22%). The nature of ring A was deduced as for the diether (IX). The presence of the free hydroxyl group was confirmed by IR and NMR spectra. Finally, the positions of the signals in the NMR spectrum due to methyl groups were identical for the diether (IX) and the new ether (VIII) pointing to the presence of the same skeletal arrangement in each.

The final minor product (ca. 5%) was assigned the 2′-hydroxyethyl 5-methyl-3,4-seco-A-homo-B-nor-5β-cholestan-4a-on-3-oate (Xa) structure. The structure of the ester portion rests upon essentially the same IR and NMR evidence as for diene-ester (IIa). The 5α-acetyl group was characterized by the IR spectrum (1689 and 1345 cm^{-1}) and the presence of a sharp three-proton singlet (τ 7·80) in the NMR spectrum. The stereochemistry at C-5 was assigned on the basis of the probable genesis of the compound. It seems probable that the compound is formed from the 3,3-ethylenedioxy-4a-ketone (V) by a series of electron shifts (cf. Fig. 2) analogous to those proposed for the formation of the diene-ester (IIa). Reaction of the keto-ester (Xa) with a trace of

[4] D. N. Kirk and V. Petrow, *J. Chem. Soc.* 4657 (1960).



hydrochloric acid in methanol again achieved exchange of the methyl group for the 2′-hydroxyethyl group initially present.

It is pertinent at this point to consider the mode of formation of the products from the 6β-methyl-5α,6α-epoxide (IV). It seemed probable that the 3,3-ethylenedioxy-4a-ketone (V) was the precursor of the remaining products (VI, VIII, IX and X). Accordingly it was found that very brief reaction of the epoxide (IV) with boron trifluoride etherate in benzene gave a high yield (>70%) of the 3,3-ethylenedioxy-4a-ketone (V). Furthermore, reaction of this ketone (V) with boron trifluoride in benzene gave (TLC)[3] the other products (VI, VIII and IX) of the epoxide-boron trifluoride reaction. Finally, reaction of the 3,4a-diketone (VI) with ether (VIII) in the presence of boron trifluoride was shown[3] (TLC) to give the diether (IX).

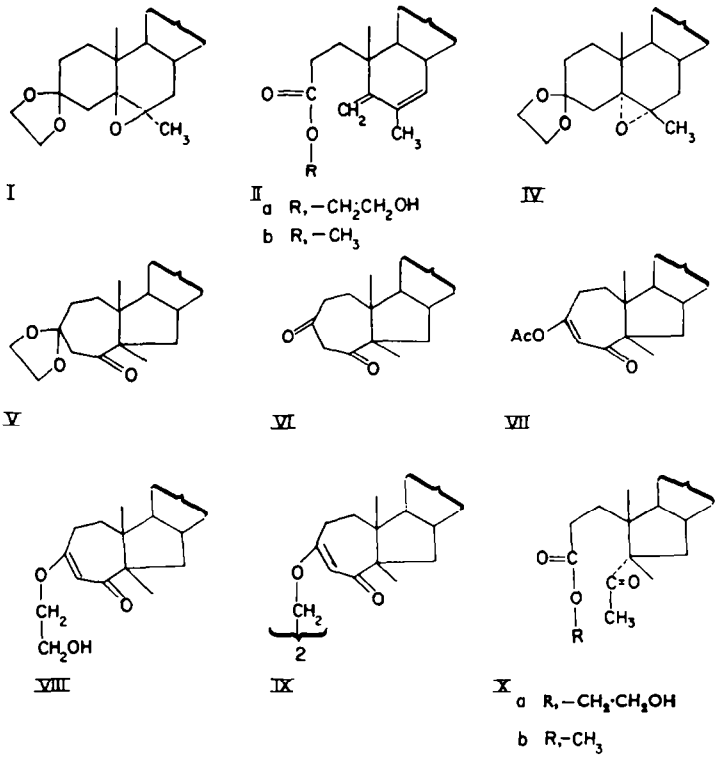
Reduction of the 3,3-ethylenedioxy-4a-ketone (V) with sodium borohydride gave an alcohol assigned the 3,3-ethylenedioxy-4a-ol (XIa) structure on the basis of IR and NMR spectra. Hydrolysis of the 3,3-ethylenedioxy-4a-ol (XIa) gave the 3-keto-4a-hydroxy compound (XIb) also obtained from the ether (VIII) by reduction with sodium borohydride followed by acid hydrolysis. The structure of the 3-keto-4a-hydroxy compound (XIb) followed from the methods of preparation supported by IR and NMR spectra. Due to the flexible nature of the seven membered ring A (Dreiding molecular models) no assignment of the stereochemistry at C-4a could be made either from a consideration of the 4a-ketone reduction process or from the NMR spectra of the 4a-hydroxy derivatives. Oxidation of the 3-keto-4a-hydroxy compound (XIb) gave the known 3,4a-diketone (VI).

6α-Hydrogen-5β,6β-epoxide

Epoxidation of 3,3-ethylenedioxycholest-5-ene, and chromatography of the product, gave the known 3,3-ethylenedioxy-5β,6β-epoxide (XIIa) and 3,3-ethylenedioxy-5α-cholestane-5,6β-diol (XIIIa). Acidic hydrolysis of the ketal-diol (XIIIa) gave the known 3-keto-5α,6β-diol (XIIIb), which on oxidation yielded the known 5α-hydroxy-3,6-diketone. The 5α,6β-diol (XIIIa) is assumed to have arisen by hydrolysis of the 3,3-ethylenedioxy-5α,6α-epoxide on the alumina used for chromatography.

Reaction of the 5β,6β-epoxide (XIIa) with boron trifluoride in benzene gave a mixture separable into five main fractions by chromatography. A non-polar gum eluted first was shown (IR, UV and TLC) to consist largely of cholesta-4,6-dien-3-one (8%) contaminated with traces of 3,3-ethylenedioxy-5α-cholestan-6-one (XIV). The major product (43%) eluted next was the ketal–ketone (XIV), the structure of which was deduced from its IR and NMR spectra and confirmed by acidic hydrolysis to give the known 5α-cholestane-3,6-dione. The third fraction (7%) was shown (IR, m.p. and mixed m.p.) to be 5α-cholestane-3,6-dione.

A minor product (6%) was assigned the diene-ester structure (XV). The ester



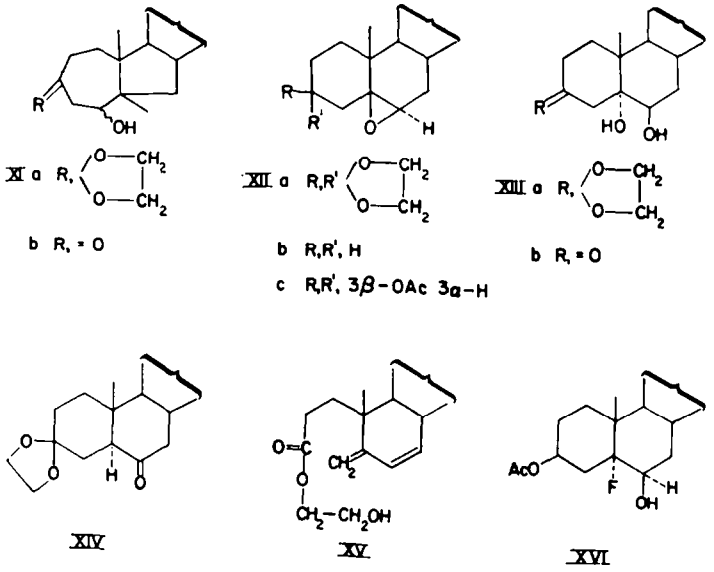
portion was characterized on the basis of IR and NMR data similar to that obtained for the 6-methyl-diene-ester (IIa) reported above. The diene structure was supported by the IR spectrum (1626, 1595 and 887 cm^{-1}) and the UV spectrum (λ_{max} 229 mμ (ε 17,800), 235 mμ (ε 19,900) and 243 mμ (ε 13,300)). In addition the NMR spectrum exhibited signals: C_4-methylene protons (τ 5·19 and 5·10), C_6–H and C_7–H (τ 4·53, 4·37, 4·08 and 3·93; equivalent to two protons).

Finally, an unsaturated alcohol (10%) was eluted the structure of which is not known.

The predominant formation of 5α-hydrogen-6-ketone structures from the 3,3-ethylenedioxy-5β,6β-epoxide (XIIa) must be explained in the context of the formation of cholestan-6-one from the 3-deoxy-5β,6β-epoxide (XIIb) and the 5α-fluoro-6β-hydroxy-compound (XVI) from the 3β-acetoxy-5β,6β-epoxide (XIIc). These observations may be rationalized in terms of the inductive effect (–I) and the steric effect of the C_3-substituent. The rearrangement of the 3-deoxy-5β,6β-epoxide (XIIb) should proceed by cleavage of a tertiary carbon-oxygen bond rather than a secondary carbon-oxygen bond, with the 1,2-shift of the C_6–H. This mode of cleavage conforms to the "axial cleavage" pattern developed[5] in an earlier paper. In the reaction of the 3β-acetoxy-5β,6β-epoxide (XIIc) the inductive effect of the 3β-acetoxy group (probably co-ordinated with boron trifluoride) will tend to oppose the C_5–O bond cleavage process to the point where the intervention of an attacking external mucleophilic, fluoride ion, would provide a lower energy route to products. However, for the 3,3-ethylenedioxy-5β,6β-epoxide (XIIa) the shielding of the α-face

at C_5 by the ketal left 6-ketone formation as the most favourable reaction, even though this is opposed by the –I effect of the ketal. It is clear that the reaction involving cleavage of ring A, although less favourable than the 1,2-hydride shift for epoxide (XIIa), becomes a major reaction in the 6-methyl-5β,6β-epoxide (I). This may reflect the greater migratory aptitude of hydrogen compared with a methyl group and/or the larger non-bonded interaction in the transition state between the migrating group and the $C_{3\alpha}$–O bond of the ketal for the 6α-methyl as opposed to the 6α-hydrogen reactions.

These various results provide a further example of the acute dependence of the reaction path upon the interplay[5] of electronic and conformational effects.



EXPERIMENTAL

Rotations were measured for $CHCl_3$ solutions at room temp. IR spectra were recorded for CS_2 solutions (unless otherwise stated) on a Perkin Elmer 221 spectrometer. UV spectra were recorded for EtOH solutions. Alumina used for chromatography was P. Spence, Grade H. "Deactivated alumina" refers to Grade H deactivated by the addition of 5% of 10% acetic acid. Light petroleum refers to the fraction of b.p. 50–70°. ORD curves (in MeOH) were kindly determined by Professor W. Klyne. NMR spectra were determined at 60 Mc in either $CDCl_3$ or CCl_4 (as stated) with $CHCl_3$ and $(CH_3)_4Si$ as internal standards.

3,3-*Ethylenedioxy-6-methylcholest-5-ene*

6β-Methyl-5α-cholestan-3β,5-diol (6·3 g) in acetone (300 ml) was treated with 8N-chromic acid[6] (4·5 ml). Addition of aqueous sodium metabisulphite gave 5-hydroxy-6β-methyl-5α-cholestan-3-one which was dehydrated to 6β-methylcholestenone on treatment with ethanolic KOHaq at 20° for 6 hr. The crude product, ethylene glycol (8·25 ml) and toluene-*p*-sulphonic acid (60 mg) in benzene (150 ml) were heated under reflux with a water separator for 5 hr. The crude product, isolated by use of ether, was crystallized from ether–MeOH to give the *ketal* (5·41 g) as needles, m.p. 148–149°, $[\alpha]_D$ −30° (*c* 1·0) ν_{max} 1112 and 1092 cm^{-1}. (Found: C, 80·6; H, 11·3. $C_{30}H_{50}O_2$ requires: C, 81·4; H, 11·4%.)

[5] M. P. Hartshorn and D. N. Kirk, *Tetrahedron* **21**, 1547 (1965).

[6] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

Epoxides of 3,3-*ethylenedioxy*-6-*methylcholest*-5-*ene* (I and IV)

The olefin (5·4 g) in $CHCl_3$ (40 ml) was treated with monoperphthalic acid (2·46 g) in ether (60 ml) for 2 hr at 20°. The solution was poured into 5% Na_2CO_3aq and the crude product isolated with ether adsorbed on deactivated alumina (250 g). Elution with benzene (5–10%)–light petroleum and crystallization from ether–MeOH gave the *β-epoxide* (I; 2·07 g) as needles, m.p. 171–171·5°, $[\alpha]_D$ +7° (*c* 1·0) ν_{max} 1115 and 1099 cm^{-1}. (Found: C, 79·0; H, 11·15. $C_{30}H_{50}O_2$ requires: C, 78·6; H, 10·9%.)

Elution with benzene and crystallization from ether–EtOH gave the *α-epoxide* (IV; 2·2 g) as an amorphus solid, m.p. 148 and 158°, $[\alpha]_D$ −27° (*c* 1·0) ν_{max} 1112 and 1094 cm^{-1}. (Found: C, 78·1; H, 11·1. $C_{30}H_{50}O_2$ requires: C, 78·6; H, 10·9%.)

3,3-*Ethylenedioxy*-5,6*β*-*epoxy*-5*β*-*cholestane* (XIIa)

3,3-Ethylenedioxycholest-5-ene (15 g) in $CHCl_3$ (140 ml) was treated with monoperphthalic acid (9 g) in ether (210 ml) for 4 days at 0°. The crude product isolated by use of ether was adsorbed on deactivated alumina (600 g). Elution with benzene-light petroleum (1:2) and crystallization from MeOH gave the *β*-epoxide (XIIa; 4·4 g) as needles, m.p. 124–126°, $[\alpha]_D$ +14° (*c* 1·0) (lit.[7]: m.p. 126–127°, $[\alpha]_D$ +9°).

Elution with ether–benzene (1:2) and crystallization from benzene gave the ketal-diol (XIIIa; 8·1 g) as an amorphous solid, m.p. 138–139°, $[\alpha]_D$ −13° (*c* 1·0). ν_{max} (nujol) 3500 (OH), 1089 and 1105 cm^{-1} (ketal). Hydrolysis of the ketal-diol gave 5,6*β*-dihydroxy-5*α*-cholestan-3-one as needles (from acetone) m.p. 220–225°, $[\alpha]_D$ +21° (*c* 1·0) (lit.[8]: m.p. 221–223°, $[\alpha]_D$+19).

Reactions of epoxides with boron trifluoride

The general procedure was as follows: The epoxysteroid, as a 4% solution in anhydrous benzene was treated with freshly-distilled BF_3-etherate (0·8 ml per 1 g steroid). After a suitable reaction time at 20°, the solution was poured into sat. $NaHCO_3$aq and the product isolated by use of ether.

Rearrangement of 3,3′-*ethylenedioxy*-5,6*β*-*epoxy*-6*α*-*methyl*-5*β*-*cholestane* (I)

The reactions was allowed to proceed for 2 min. The isolated product was adsorbed onto deactivated alumina (50 g). Elution with light petroleum–benzene (9:1) gave 6-methylcholesta-4,6-dien-3-one as needles from MeOH (42%) m.p. and mixed m.p. 90–92°, $[\alpha]_D$ +34° (*c* 1·0), λ_{max} 290 mμ (log ε 4·37) (lit.[9]: 91–92°, $[\alpha]_D$ +37°, λ_{max} 290 mμ (log ε 4·38).

Fractions eluted by benzene gave the *diene-ester* (IIa; 44%) as a gum (pure by TLC) $[\alpha]_D$ −36° (*c* 1·35), ν_{max} (liquid film) 3333 (OH), 1730 and 1176 (ester), 1592 and 890 cm^{-1} (diene), λ_{max} 233 mμ (ε 20,500), 239 mμ (ε 23,000), 246 mμ (ε 15,700), NMR ($CDCl_3$) as quoted in discussion and τ 9·27 ($C^{18}H_3$), τ 9·03 ($C^{19}H_3$) and τ 9·08 and 9·18 (side chain CH_3). (Found: C, 78·2; H, 11·2. $C_{30}H_{50}O_2$ requires: C, 78·6; H, 10·9%.)

Diene methyl ester (IIb)

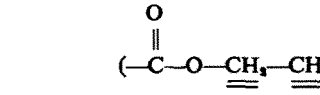
Reaction of IIa with MeOH containing a trace of 12N HCl for 7 hr at 20° gave a crude product separable into two fractions by chromatography on deactivated alumina. Apart from IIa (65%) the methyl ester (IIb), was isolated as a gum, ν_{max} (liquid film) 1745, 1174 (ester, 1595 and 887 cm^{-1} (diene), λ_{max} 235 mμ (ε 21,400) 240 mμ (ε 23,900) 247 mμ (ε 16,300), NMR ($CDCl_3$ 4·44 (C^7–H), τ 4·97 and 5·03 (C^6-methylene protons), τ 6·33 (ester CH_3), τ 7·83 (−C^3–H_2−), τ 8·17 (C^6–CH_3) τ 9·28 ($C^{18}H_3$), τ 9·05 ($C^{19}H_3$) and τ 9·08 and 9·18 (side chain CH_3).

Ethylene glycol monobutyrate.[10]

A mixture of n-butyric acid (45 ml), ethylene oxide (100 ml) and KOH (1·1 g) in water was kept at 15° for 5 days. Isolation by means of ether followed by distillation gave the hydroxy-ester, b.p. (20 mm) 110–116°, shown by GLC to contain n-butyric acid (5%), ν_{max} (liquid film) 3390 cm^{-1} (OH), 1740 and 1182 cm^{-1} (ester), NMR (CCl_4) τ 5·88 (—C(=O)—O—CH_2CH_2OH), τ 6·20 (—C(=O)—O—CH_2—CH_2OH).

[7] G. Cooley, B. Ellis, D. N. Kirk and V. Petrow, *J. Chem. Soc.* 4112 (1957).
[8] F. Bottari and B. Macchia, *Gazz. Chim. Ital.* **90**, 1783 (1960).
[9] B. Ellis, D. N. Kirk, V. Petrow, B. Waterhouse and D. M. Williamson, *J. Chem. Soc.* 2828 (1960).
[10] H. Fraenkel-Conrat and H. S. Olcott, *J. Amer. Chem. Soc.* **66**, 1420 (1944).

Acetylation of the hydroxy-ester using acetic anhydride–pyridine at 20° for 12 hr gave ethylene glycol monoacetate-monobutyrate, ν_{max} (liquid film) 1745, 1227 and 1182 cm^{-1}, NMR (CCl_4) τ 5·80



Rearrangement of 3,3-*ethylenedioxy*-5,6α-*epoxy*-6β-*methyl*-5α-*cholestane* (IV)

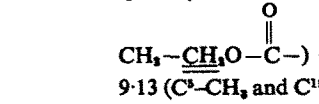
(a) The reaction of epoxide (450 mg) in benzene (11 ml) with BF_3-etherate (0·4 ml) was allowed to proceed for 30 sec. The crude product, crystallized from MeOH, gave the *ketal-ketone* (V; 325 mg), m.p. 128–129°, $[\alpha]_D$ +12° (*c* 1·0), ν_{max} 1698, 1088 cm^{-1}, ORD $[\phi]_{330}$ +600°, $[\phi]_{285}$ −200°. (Found: C, 78·8; H, 11·0. $C_{30}H_{50}O_3$ requires: C, 78·6; H, 10·9%.) NMR ($CDCl_3$) τ 6·11 and 6·07 (—O—CH_2—CH_2—O—), τ 6·73, 6·91, 7·43 and 7·60 (—C^4H_2—), τ 9·34 ($C^{18}H_3$), τ 9·03 and 8·81 (C^5–CH_3, $C^{19}H_3$) τ 9·20 and 9·10 (side chain CH_3).

(b) The epoxide (1 g) in benzene (25 ml) was treated with BF_3-etherate (0·85 ml) for 3·5 min. The isolated product was adsorbed onto deactivated alumina (50 g). Elution with light petroleum-benzene (4:1) gave a mixture (430 mg) of two compounds (TLC) which gave on crystallization from pentane V (84 mg), m.p. 128–129°, $[\alpha]_D$ +12° (*c* 1·0). Hydrolysis of the residue from the crystallization with AcOHaq gave the 3,4a-*diketone* (VI) as an amorphus solid of indeterminate m.p. $[\alpha]_D$ −50° (*c* 0·43), ν_{max} (CCl_4) 1718, 1689, 1445 and 1408 cm^{-1}, λ_{max} (EtOH–KOH) 301 mμ (ε 21,000) NMR (CCl_4) τ 6·51 (—C^4H_2—), τ 9·37 ($C^{18}H_3$), τ 9·10 and 8·87 (C^5–CH_3 and $C^{19}H_3$), τ 9·10 and 9·20 (side chain-CH_3). The composition of the original column eluent was estimated (UV in EtOH–KOH) as V (270 mg; 27%) and VI (160 mg; 16%).

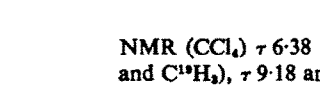
Light petroleum–benzene (1:1) eluted the *di-ether* (IX) (230 mg; 23%) as needles (from Et_2O), m.p. 219–219·5°, $[\alpha]_D$ −112° (*c* 1·11). M.W. (Rast) Found: 780, calc. 854. ν_{max} (CS_2) 1653, 1629 and 1182 cm^{-1}, λ_{max} 255 mμ (23,000) (Found: C, 81·4; H, 11·1. $C_{58}H_{94}O_4$ requires: C, 81·5; H, 11·0%) NMR ($CDCl_3$) τ 4·78 (C^4–H), τ 6·05 (—O—CH_2—CH_2—O—), τ 9·37 ($C^{18}H_3$), τ 9·07 and 8·83 (C^5–CH_3 and $C^{19}H_3$), τ 9·10 and 9·20 (side chain CH_3). Hydrolysis of the di-ether with AcOHaq gave the 3,4a-diketone.

Elution with benzene–ether (20:1) gave the *hydroxy-ether* (VIII; 220 mg; 22%) as a gum (pure by TLC), $[\alpha]_D$ −84° (*c* 1·1), ν_{max} (CS_2) 3590, 1645, 1626 and 1185 cm^{-1}, λ_{max} 255 mμ (ε 11,000) NMR $CDCl_3$) τ 4·81 (C^4–H), τ 6·20 (—O—CH_2—CH_2—O—), τ 5·83 (OH; removed by D_2O), τ 9·37 ($C^{18}H_3$), τ 9·07 and 8·83 (C^5–CH_3 and $C^{19}H_3$) τ 9·10 and 9·20 (side chain CH_3).

Further elution with benzene–ether (20:1) gave the *A-seco-compound* (Xa; 54 mg; 5%) as a gum (pure by TLC) ν_{max} (liquid film) 3390, 1735, 1690, 1345 and 1175 cm^{-1}, NMR ($CDCl_3$) τ 5·87 (HO—



τ 6·20 (HOCH_2CH_2—O—), τ 7·80 (), τ 9·35 ($C^{18}H_3$), τ 8·83 and 9·13 (C^5–CH_3 and $C^{19}H_3$), τ 9·10 and 9·20 (side chain CH_3). Reaction of Xa with MeOH containing a trace of HCl (12N) at 20° for 17 hr gave Xb as a gum, ν_{max} (CCl_4) 1735, 1690, 1350 and 1170 cm^{-1},



NMR (CCl_4) τ 6·38 (), τ 7·83 (), τ 9·35 ($C^{18}H_3$), τ 8·83 and 9·13 (C^5–CH_3 and $C^{19}H_3$), τ 9·18 and 9·09 (side chain CH_3).

Reduction of ketal-ketone (V)

A solution of V (55 mg) and $NaBH_4$ (15 mg) in MeOHaq containing a trace of NaOH was kept at 20° for 30 min. The ketal-alcohol (XIa) had ν_{max} (CS_2) 3460, 1109 and 1087 cm^{-1}. Reaction of XIa with acetone containing toluene-*p*-sulphonic acid gave the 3-*keto*-4a-*hydroxy compound* (XIb), as needles from MeOH, m.p. 185–187°, $[\alpha]_D$ +6° (*c* 1·0), ν_{max} (CS_2) 3550, 3400, 1698 cm^{-1}. (Found: C, 81·0; H, 11·9. $C_{28}H_{48}O_3$ requires: C, 80·8; H, 11·5%.) NMR ($CDCl_3$) τ 6·30 (C^{4a}–H), τ 9·33 ($C^{18}H_3$), τ 9·07 and 9·00 (C^5–CH_3 and $C^{19}H_3$), τ 9·10 and 9·20 (side chain CH_3).

Oxidation of XIb with 8N-chromic acid[6] in acetone gave the known 3,4a-diketone.

Reduction of VIII

Reaction of VIII with $NaBH_4$ in MeOHaq containing a trace of NaOH under reflux for 2 hr followed by treatment of the crude product with acetone–toluene-*p*-sulphonic acid gave XIb as needles, m.p. and mixed m.p. 185–188°, IR identical with the sample prepared above.

Enol-acetylation of the 3,4a-*diketone* (VI)

Reaction of VI in pyridine–acetic anhydride at 20° for 5 days gave the *enol acetate* (VII) as needles from MeOH, m.p. 133–133·5°, $[\alpha]_D$ −42° (*c* 1·0), ν_{max} (CS_2) 1754, 1667, 1254, 1198 cm^{-1}, λ_{max} 230 mμ (ε 5,000) (Found: C, 78·2; H, 10·9. $C_{30}H_{48}O_3$ requires: C, 78·9, H, 10·5%) NMR (CCl_4) 4·40 (C^4–H), τ 7·88 (CH_3—C(=O)—O), τ 9·35 ($C^{19}H_3$), τ 9·03 and 8·78 (C^5–CH_3 and $C^{18}H_3$), τ 9·18 and 9·09 (side chain CH_3). Lit. values for spiran-25D series analogue[4], ν_{max} (CCl_4) 1760, 1672 cm^{-1}, λ_{max} 230·5 mμ (ε 7,170).

Rearrangement of 3,3-*ethylenedioxy*-5,6β-*epoxy*-5β-*cholestane* (XIIa)

The epoxide (1 g) in benzene (25 ml) was treated with BF_3-etherate (0·8 ml) for 2 min. The isolated product was adsorbed onto deactivated alumina (50 g). Elution with light petroleum–benzene (9:1) gave impure (ca. 80%) cholesta-4,6-dien-3-one (12%) as a gum ν_{max} (liquid film) 1669, 1618 and 1590 cm^{-1}, λ_{max} 285 mμ (ε 19,000) (lit.[11]: λ_{max} 285 mμ (ε 26,000).

Elution with light petroleum–benzene (3:1) gave XIV (43%) as needles from acetone, m.p. 126–127°, $[\alpha]_D$ −10° (*c* 1·0), ν_{max} (CCl_4) 1718, 1111 and 1096 cm^{-1}. (lit.[12]: m.p. 124–126°, $[\alpha]_D$ 0° (dioxan)). Hydrolysis of XIV gave the known 5α-cholestane-3,6-dione, m.p. and mixed m.p. 173–174°, $[\alpha]_D$ +8° (*c* 1·0).

Elution with light petroleum–benzene (1:1) gave 5α-cholestane-3,6-dione (13%) as needles (from acetone), m.p. and mixed m.p. 173–174°, $[\alpha]_D$ +8° (*c* 1·0).

Elution with benzene gave XV (6%) as a gum, ν_{max} (liquid film) 3356, 1724, 1626, 1595, 1178 and 887 cm^{-1}, λ_{max} 229 mμ (ε 17,800), 235 mμ (ε 19,900) and 243 mμ (ε 13,300), NMR (CCl_4) as quoted in discussion and τ 9·27 ($C^{18}H_3$), τ 9·03 ($C^{19}H_3$), τ 9·17 and 9·08 (side chain CH_3).

Finally elution with benzene–ether (9:1) gave an unsaturated alcohol (10%) as needles from hexane, m.p. 124–126°, $[\alpha]_D$ −6° (*c* 1·05), ν_{max} (CS_2) 3570, 1710 cm^{-1}.

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