Tetrahedron, 1964, Vol. 20, pp. 2531 to 2545. Pergamon Press Ltd. Printed in Northern Ireland

REACTIONS OF EPOXIDES—I

REARRANGEMENTS OF SOME 3-SUBSTITUTED 4,5-EPOXY-4-METHYLCHOLESTANES WITH BORON TRIFLUORIDE

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(*Received* 29 *June* 1964)

Abstract—The epimeric 4,5-epoxides derived from 4-methylcholest-4-en-3-one and 3α- and 3β-acetoxy-4-methylcholest-4-enes have been rearranged with boron trifluoride. Each of the six epoxides exhibits its own distinctive pattern of behaviour.

TRI-SUBSTITUTED epoxides in the steroid series usually undergo rearrangement to give ketones when they are treated with boron trifluoride in an inert solvent. A polar substituent in the vicinity of the epoxide group may, however, alter the course of the reaction so that a diaxial fluorohydrin becomes the main product. Henbest[1] has studied the reactions between boron trifluoride and various 5α,6α- and 5β,6β-epoxycholestanes, with and without substituents at C-3, and has interpreted the observed results in terms of the long-range inductive effect of the C-3 substituent, and the avoidance, where possible, of steric interactions involving bulky axial substituents in the product. Bowers,[2] correctly predicting the influence of 3-oxo- and 3,3-ethylenedioxy groups on the reactivity of the 5α,6α-epoxy system, was able to obtain 6β-fluoro-5α-hydroxy-steroids as intermediates in the preparation of 6-fluoro hormone analogues.

2,3-Epoxy-cyclohexanone, and some of its derivatives, have been shown[3] to rearrange on treatment with boron trifluoride, giving cyclohexane-1,2-diones, ring-contracted compounds, or mixtures of these products, depending on the presence of alkyl or phenyl substituents at C-2 or C-3. Collins[4] found that the isomeric 4,5-epoxycholestan-3-ones behave in a similar way, giving cholestane-3,4-dione and A-nor-cholestan-3-one, although in low yields.

In a recent survey of epoxide-boron trifluoride reactions, Goldsmith[5] suggested that the nature of the solvent may control the degree of development of a carbonium ion transition state, and that this should decide, in the absence of controlling steric factors, whether a ketone or a fluorohydrin is the initial product. Goldsmith considered that the subsequent transformation of a fluorohydrin into a ketonic product should occur only in open chain compounds, for a *trans*- diaxial fluorohydrin in a rigid cyclic system is unfavourably oriented for conversion into a ketone.[5]

A few unusual reactions of trisubstituted epoxides have also been reported, such

[1] H. B. Henbest and T. I. Wrigley, [a] *J. Chem. Soc.* 4596 (1957); [b] *Ibid.* 4765 (1957).
[2] A. Bowers, L. Ibáñez and H. J. Ringold, *Tetrahedron* **7**, 138 (1959).
[3] H. O. House and R. L. Wasson, *J. Amer. Chem. Soc.* **79**, 1488 (1957).
[4] D. J. Collins, *J. Chem. Soc.* 3919 (1959).
[5] D. J. Goldsmith, *J. Amer. Chem. Soc.* **84**, 3913 (1962).

as the Westphalen-type rearrangement of a 5α,6α-epoxy-B-nor-steroid,[6] and the conversion of 3β-acetoxy-4α,5α-epoxycholestane into 4β-acetoxycholestane-3β,5α-diol.[7]

Very few examples of reactions between boron trifluoride and tetra-substituted steroidal epoxides have been described. Henbest[1a] found that some epoxide rings across ring junction positions were converted into dienes. Kirk and Petrow[8] have shown that 5α,6α-epoxy-6β-methylsteroids undergo a skeletal rearrangement leading to 5β-methyl-A-homo-B-nor-4a-ketones. Another skeletal rearrangement occurs with a 9α,11α-epoxy-11β-methylsteroid, again with the formation of a ketonic product.[9]

In a tetra-substituted epoxide, ketone formation may, in principle, occur by migration of any one of the four alkyl groups or ring residues, for, in the absence of outside influences, the two C—O bonds can be considered as equally likely to break following coordination of the epoxy-oxygen with boron trifluoride. Accordingly it seemed that such a system should show high sensitivity to both steric effects and the inductive effects of nearby polar groups.

This expectation was confirmed when we studied the reactions between boron trifluoride and a series of tetra-substituted epoxides. The compounds studied were the 4α,5α- and 4β,5β-epoxy-derivatives of 4-methylcholest-4-en-3-one, and the four epimeric 3-acetoxy-4,5-epoxy-4-methylcholestanes. The preparation of these compounds by routes which establish their stereochemistry is described elsewhere.[10]

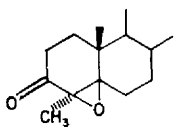
Reactions of 3-substituted-4,5-epoxy-4-methylcholestanes with boron trifluoride

The reaction conditions chosen were essentially those used by Henbest.[1] Boron trifluoride etherate was added to a solution of the epoxide in anhydrous benzene, and the reaction was allowed to proceed at room temperature. It was not possible to follow the progress of the reactions polarimetrically, for in all cases the mixtures produced translucent gels, and deep colours developed in reactions involving 3-acetoxy-4,5-epoxides. We therefore used the appearance of the system as the criterion for deciding the reaction time. For each epoxide (with one exception) we performed at least two experiments, one being terminated after a short interval (2–10 min), when the gel appeared to have reached its maximum opacity, but without appearance of deep colours. The second series of reactions with longer reaction times (20 min–5 hr) was allowed to proceed to the point where the gels had dissolved, giving clear solutions of various colours. The epoxy-ketones (I and II) rapidly formed gels, which required about 5 hr for subsequent reaction, giving pale coloured solutions. The acetoxy-epoxides formed gels in 1–5 min and the subsequent reactions were rapid, requiring only 10–45 min for the development of deep colours.

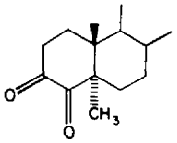
Reactions were terminated by the addition of aqueous sodium acetate or bicarbonate, and the products were separated by chromatography. The mixtures of products obtained were unexpectedly complex, as many as six different compounds

[6] W. G. Dauben, G. A. Boswell, W. Templeton, J. W. McFarland and G. H. Berezin, *J. Amer. Chem. Soc.* **85**, 1672 (1963).
[7] S. Julia and J. P. Lavaux, *Bull. Soc. chim. Fr.* 1238 (1963).
[8] D. N. Kirk and V. Petrow, *J. Chem. Soc.* 4657 (1960).
[9] W. J. Wechter and G. Slomp, *J. Org. Chem.* **27**, 2549 (1962).
[10] J. M. Coxon, M. P. Hartshorn and D. N. Kirk, *J. Chem. Soc.* 2461 (1964).

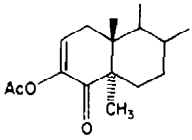
being isolated from one epoxide. We were able to isolate and characterize all the ketonic products formed in significant quantities from the six epoxides studied. Several other products containing hydroxyl groups were also characterized, but the quantities available did not allow identification of every compound isolated. As no regular pattern of behaviour was discernable, we shall describe separately our experiments with each of the six epoxides.



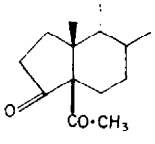
I



Ia



Ib



Ic

4β,5-Epoxy-4α-methyl-5β-cholestan-3-one (I)

Treatment of a benzene solution of the β-epoxy-ketone (I) with boron trifluoride gave a gelatinous precipitate, from which the epoxy-ketone was regenerated after 10 min by the addition of aqueous sodium acetate. If, however, the reaction mixture was left at room temperature, the gel gradually dissolved. Hydrolysis after 5½ hr gave a mixture from which two diketones were separated, each in 39% yield, by chromatography on silica gel. The first compound eluted was 5α-methylcholestane-3,4-dione (Ia), which existed in solution largely as its Δ^2-enol, as revealed by the IR spectrum. The enol acetate (Ib) was readily obtained, and its UV absorption (λ_{max} 240 mμ) confirmed the α-diketone structure. The 5α- configuration follows from the consideration (Dreiding models) of a methyl-group shift either concerted with or following the rupture of the C_5—O bond.

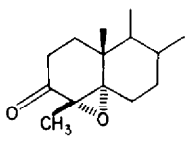
The 5-acetyl-A-nor-3-keto structure (Ic) was indicated for the second diketone by its NMR spectrum, which showed a peak at τ7·87 (three protons) due to the acetyl group. The assignment was confirmed by the IR spectrum which exhibited bands due to the five-membered ring ketone (1751 cm^{-1}) and the acetyl group (1692 and 1355 cm^{-1}). The 5β-configuration is assigned to the acetyl group from a consideration of the stereochemistry of the attack of C-3 upon C-5, assuming this to be concerted with the rupture of the C_5—O bond. The subsequent preparation of the epimeric 5-acetyl-A-nor compound (IIc) from the α-epoxy-ketone appears to support this assignment.

An intractable gum showing hydroxyl-group absorption in the IR, analysing for 2% fluorine (equivalent to ca. ½ atom), and also containing C:C unsaturation (tetranitromethane) accounted for the remainder of the material.

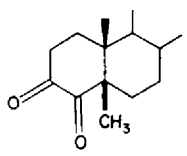
4α,5-Epoxy-4β-methyl-5α-cholestan-3-one (II)

Like the β-epoxyketone, the α-epoxyketone (II) was recovered by hydrolysis of the gel formed initially with boron trifluoride. When the reaction was prolonged until the gel had liquefied (5½ hr) the product was a mixture from which three new compounds were isolated.

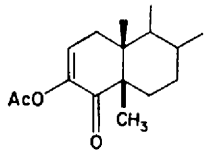
The α-diketone (IIa), obtained in 16% yield, was characterized by its absorption spectra, and by the easy formation of its Δ^2-enol acetate (IIb). A second diketone (9% yield) was identified as 5α-acetyl-A-nor-cholestan-3-one (IIc). The IR spectrum showed the presence of a 5-membered ring ketone and an acetyl group. The NMR



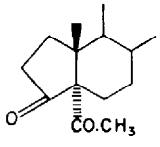
II



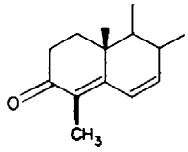
IIa



IIb



IIc



IId

spectrum exhibited a peak at τ7·87 due to the acetyl methyl group (three protons) and four peaks at lower field (τ7·67, τ7·62, τ7·52, τ7·47). The integral over this region revealed only two protons, which must be those at C-2, deshielded by the C-3 carbonyl group. The acetyl group is therefore attached at a quaternary carbon atom (C-5). The α-configuration at C-5 follows from a consideration of the stereochemistry of the ring contraction process if the attack of C-3 upon C-5 is concerted with the cleavage of the C_6-O epoxide linkage, as seems likely.

The major product isolated (25%) was 4-methylcholesta-4,6-dien-3-one (IId), which was identified from its spectroscopic properties (λ_{max} 291 mμ)[11] and by comparison with an authentic sample. This was prepared by dehydrogenation of 4-methylcholest-4-en-3-one with chloranil.[12] The identity of the two samples was confirmed by their conversion into identical 2,4-dinitrophenylhydrazones.

The remaining material from the epoxyketone reaction (46%) was a mixture of hydroxylic compounds, and contained both C:C unsaturation and fluorine. Attempts to resolve it into its components by further chromatography were unsuccessful.

3β-Acetoxy-4β,5β-epoxide (III)

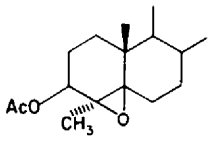
The gel formed on mixing a benzene solution of the 3β-acetoxy-β-epoxide (III) with boron trifluoride etherate began to turn pink after a few minutes. Isolation of the product at this stage gave the fluorohydrin (IIIc) by direct crystallization. When the reaction was allowed to proceed for 20 or 30 min, and the product chromatographed on deactivated alumina, five distinct compounds were isolated.

After elution of a yellow gum (7·8%) from the column, the enol acetate (IIIa) of 4-methylcholest-4-en-3-one was obtained (16%). This compound has been described previously,[13] and its structure was confirmed by comparison with an authentic sample. A small quantity (3%) of 4-methylcholest-4-en-3-one, probably arising by hydrolysis of some enol acetate on the alumina column, was eluted next. The succeeding fractions yielded a crystalline mixture of 3β-acetoxy-5α-methylcholestan-4-one (IIIb) and an unidentified acetoxy-alcohol. Re-chromatography of these fractions failed to separate the compounds, but the acetoxy-ketone (IIIb) was isolated by careful

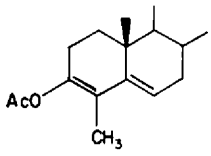
[11] D. N. Kirk, V. Petrow and M. H. Williamson, *J. Chem. Soc.* 3872 (1960).
[12] E. J. Agnello and G. D. Laubach, *J. Amer. Chem. Soc.* **79**, 1257 (1957).
[13] N. W. Atwater, *J. Amer. Chem. Soc.* **82**, 2847 (1960).

fractional crystallization from methanol, in which the acetoxy-alcohol was slightly more soluble. The structure of the α-acetoxy-ketone followed from its IR spectrum, which showed the usual frequency shift of both the acetoxy and ketone carbonyl stretching absorptions.[14] The O.R.D. curve showed a negative Cotton effect of the right order of amplitude ($a = -43$), consistent with a positive increment for the 5α-methyl group as required by the octant rule,[15] superimposed upon the large negative amplitude ($a = -94$) for 5α-cholestan-4-one.[16] The 3β-acetoxy group, being equatorial, should make little contribution to the amplitude. The wavelengths at the extrema (307 and 264 mμ) support the equatorial acetoxy assignment.[17] The NMR spectrum, which is in full agreement with the assigned structure, is discussed later. The fluorohydrin (IIIc) was eluted next (10%), and proved to be identical with the material obtained as the main product from the brief reaction between the epoxide and boron trifluoride. Its structure was indicated by elemental analysis and supported by the regeneration of the original β-epoxide by alkaline hydrolysis followed by reacetylation. The 5α-fluoro-4β-hydroxy structure (IIIc) is preferred to the 4α-fluoro-5β-hydroxy alternative, which would involve larger steric interactions between axial substituents, as revealed by the study of Dreiding models. Evidence supporting the 5α-fluoro-4β-hydroxy-structure was obtained by submitting the compound to mild alkaline hydrolysis, and oxidizing the resulting 5α-fluoro-3β,4β-diol with sodium metaperiodate. The IR spectrum of the crude product exhibited bands due to aldehyde and acetyl groups, indicating that ring cleavage had occurred to give a product formulated as the A-seco compound (IIId).

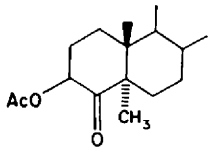
The final material (19%) from the epoxide rearrangement formed low-melting solvated crystals. Elemental analysis was indecisive but suggested the presence of only one hydroxyl group. The IR spectrum confirmed the presence of acetoxy and hydroxy- functions, but the structure of the compound is unknown.



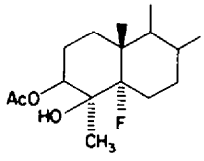
III



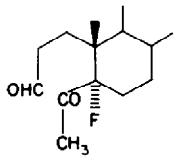
IIIa



IIIb



IIIc



IIId

[14] R. N. Jones and F. Herling, *J. Org. Chem.* **19**, 1252 (1954).
[15] C. Djerassi, *Optical Rotatory Dispersion* McGraw-Hill, New York (1960).
[16] C. Djerassi, W. Closson and A. E. Lippman, *J. Amer. Chem. Soc.* **78**, 3163 (1956); C. Djerassi and W. Klyne, *J. Chem. Soc.* 2390 (1963).
[17] C. Djerassi, O. Halpern, V. Halpern, O. Schindler and C. Tamm, *Helv. Chim. Acta* **41**, 250 (1958).

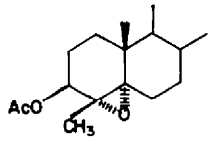
3β-Acetoxy-4α,5α-epoxide (IV)

Brief reaction with boron trifluoride gave a gelatinous precipitate which was hydrolysed after 2 min. The product was a mixture which yielded unreacted epoxide (30%), the 4β,5α-diol (IVc; 26%), and an unidentified hydroxy-compound which was isolated only as a gel. The latter compound analysed as a triol monoacetate, and was not affected by chromic acid-acetone.

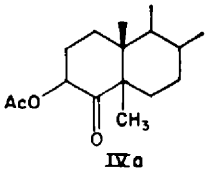
When the reaction time was extended to 25 min the initially formed gelatinous precipitate dissolved to give a deep purple solution from which six distinct compounds were obtained. The products were separated by chromatography. The first compound isolated (8%) showed only acetoxy- absorption in the IR spectrum. Despite a similarity between the physical properties of this compound and the original epoxide, there was a depression in m.p. of the mixture, and the IR spectra showed differences in the "fingerprint" region. The NMR spectrum revealed no vinylic protons. Alkaline hydrolysis, followed by oxidation with chromic acid in acetone, gave a non-conjugated 6-membered ring ketone (ν_{max} 1710 cm^{-1}). The structures of these products are unknown.

Two acetoxy-ketones were isolated next. The first (10%) was 3β-acetoxy-5-methyl-5β-cholestan-4-one (IVa), characterized by its IR spectrum. The O.R.D. curve showed a strongly negative Cotton effect ($a = -124$), with extrema at 338 and 286 mμ, confirming the axial conformation of the acetoxy[17] group, even though in a chair conformation of ring A this involves an appreciable non-bonded interaction between the acetoxy group and the 5β-methyl group. The NMR spectrum is discussed below.

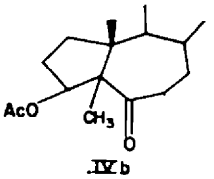
The second acetoxy-ketone (26%) showed IR absorption due to isolated acetoxy- and keto- groups (1748 and 1701 cm^{-1}), suggesting the A-nor-B-homo- structure (IVb). The possible alternative 5-acetyl-A-nor- structure was excluded by the absence of IR absorption at about 1356 cm^{-1}, and by the absence of a low-field methyl signal in the NMR spectrum, apart from the band due to the three protons of the 3β-acetoxy group. The skeletal rearrangement leading to the A-nor-B-homo-structure (IVb) was confirmed when the acetoxy ketone was hydrolysed and oxidized to give a diketone (IVd) having the IR absorption bands for both 5- and 7-membered ring ketones. The 5β-methyl configuration is assigned to these compounds from a consideration of the stereochemistry of the rearrangement process.



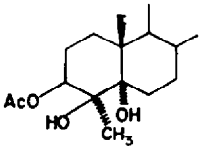
IV



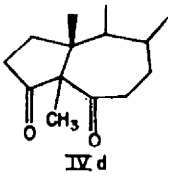
IVa



IVb



IVc



IVd

Further elution from the column gave an acetoxy-alcohol, m.p. 103–103·5° (26%). Elemental analysis indicated the formula $C_{30}H_{50}O_3$, corresponding to the original acetoxy-epoxide, and the presence of a tetrasubstituted olefinic double bond was revealed by an intense colour reaction with tetranitromethane, and the absence of a vinyl proton signal in the NMR spectrum. The hydroxyl group was shown to be tertiary from its failure to oxidize or acetylate, while alkaline hydrolysis of the acetoxy group was rather slow, requiring 5 days at 20° or 2 hr reflux in 5% methanolic potassium hydroxide. The resulting diol, which reverted to the acetoxy-alcohol on acetylation, was oxidized by chromic acid–acetone to give a hydroxy-ketone. The IR spectrum showed this to be a non-conjugated six-membered ring ketone, and treatment with methanolic hydrochloric acid did not alter the carbonyl absorption. The structures of these compounds are obscure.

The final product (9%) from the reaction of the epoxide was the 4β,5α-diol (IVc), which has been prepared previously by acid-catalysed hydrolysis of the epoxide.[7]

3α-Acetoxy-4β,5β-epoxide (V)

When the epoxide was allowed to react with boron trifluoride for only 2 min the major reaction product (36%) was the 4β,5α-diol (Va) presumably derived by hydrolysis of the epoxide-boron trifluoride complex. Both hydroxyl groups were shown to be tertiary by the failure of chromic acid–acetone to oxidize the diol. Apart from unreacted epoxide (40%) the only other product found was an unsaturated acetoxy-alcohol (18%). The structure of this compound cannot be regarded as fully established but the evidence available suggests that it is 3α-acetoxy-4α-methylcholest-5-en-4β-ol (Vc). The hydroxy-group was not oxidizable. The negative specific rotation ($[\alpha]_D$ −46°) is characteristic of Δ^5-steroids. The NMR spectrum revealed the presence of an olefinic proton (τ4·17), and showed other bands due to the C-3 proton (τ5·13), and the acetoxy-methyl group (τ7·95). A low field methyl signal (τ8·68) is tentatively assigned to the 4α-methyl group, for it was shifted (τ8·37) on hydrolysis of the 3-acetoxy group. The spectrum of the diol also exhibited the olefinic proton (τ4·12), and the C-3 proton appeared as a doublet centred at τ6·40 (J_{HH} = 12 c/s).

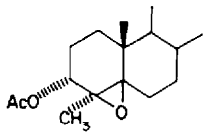
A band at τ8·77 in both the 3-acetate and the diol is tentatively assigned to the C-19 methyl group, the unusually large down-field shift being compatible with the combined deshielding effect of the 4β-hydroxyl and Δ^5-functions.[18] Additional evidence for the Δ^5-structure was adduced from the oxidation of the 3,4-diol with sodium metaperiodate. The crude product was a dicarbonyl compound with the IR and UV spectroscopic features expected for the unsaturated keto-aldehyde structure (Vd).

When the reaction between the epoxide and boron trifluoride was prolonged the mixture quickly became deep blue, and chromatography of the products obtained after either 1·5 hr or 5 hr gave four distinct fractions. The first was non-polar material of unknown composition (6% in 1·5 hr; 13% in 5 hr). This was followed by the 3α-acetoxy-4β,5β-epoxide (V) in ca. 40% yield, irrespective of the reaction time. The constancy of this proportion of epoxide is remarkable, and suggests that it may have arisen from decomposition of a reactive fluorohydrin on the column of alumina. 3α-Acetoxy-5α-methyl-cholestan-4-one (Vb) eluted next (29% in 1·5 hr; 22% in 5 hr) was characterized by its IR absorption. The structure was supported by its NMR

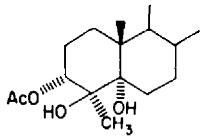
[18] R. F. Zurcher, *Helv. Chim. Acta* **46**, 2054 (1963).

spectrum (see below), and the O.R.D. curve ($a = +62$), with extrema at 332·5 and 290 mμ confirmed the axial conformation of the 3α-acetoxy group.[17]

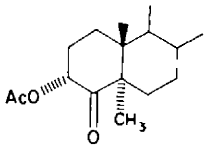
The more polar fractions afforded a small quantity (11%) of the unsaturated acetoxy-alcohol (Vc).



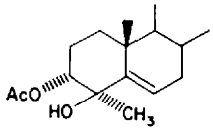
V



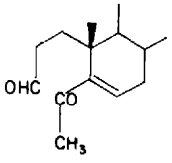
Va



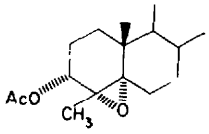
Vb



Vc



Vd



VI

3α-Acetoxy-4α,5α-epoxide (VI)

Only a very small sample of this epoxide was available.[10] It reacted with boron trifluoride to give essentially a single acetoxy-alcohol of unknown structure. A strong positive reaction with tetranitromethane indicated unsaturation, but no vinylic proton appeared in the NMR spectrum, thereby excluding a Δ^5-structure. It is noteworthy that this epoxide gave no ketonic product.

The NMR spectra of the 3-acetoxy-5-methylcholestan-4-ones (IIIb, IVa and Vb) showed low field signals (see Table 1) due to the C-3 proton, a peak at τ7·85–7·95 due

TABLE 1. NMR SPECTRA OF α-ACETOXY-KETONES

C-3 proton signals in α-acetoxy-ketones				
Cholestan-4-one derivative	Conformation of C-3 proton	C-3 Proton signal τ	splitting	J_{HH} (c/s) (estimated)
3β-OAc, 5α-Me (IIIb)	a	4·43	Indistinct quadruplet	8, 12
3α-OAc, 5α-Me (Vb)	e	4·78	Quadruplet (irregular)	3, 8
3β-OAc, 5β-Me (IVa)	e	4·95	Triplet (barely resolved	2·5
3β-OAc, 5α-H	a	4·83	Quadruplet	6·5, 11·5

to the three protons of the acetoxy methyl group, and the normal peaks due to the cholestane skeleton. Data reported by Williamson and Johnson[19] for other steroidal α-acetoxy-ketones show that the chemical shift for an equatorial proton adjacent

[19] K. L. Williamson and W. S. Johnson, *J. Amer. Chem. Soc.* **83**, 4623 (1961).

to the acetoxy group is larger than for a similar axial proton, an observation which has recently been rationalized[20] in terms of the resultant dipole moment of the acetoxy-ketone system. The τ values reported in Table 1 therefore serve to confirm the structures assigned to the 3-acetoxy-5-methyl-cholestan-4-ones. The irregular quadruplet exhibited by the 3β-acetoxy-5α-methyl isomer (IIIb) was almost identical in profile with the quadruplet in the spectrum of 3β-acetoxy-5α-cholestan-4-one,[21] which is included in Table 1 for comparison. The spin-spin coupling constants approximate to those reported[19] for 2α-acetoxy-5α-cholestan-3-one and 3β-acetoxy-5α-cholestan-2-one, revealing a moderate distortion of ring A from the pure "chair" form. The observation of an irregular quadruplet for the C-3 proton in the 3α-acetoxy-5α-methyl isomer (Vb) shows that here the C-2 protons are non-equivalent with respect to the equatorial C-3 proton. The modified Karplus equation used by Williamson and Johnston[19] gives impossible values for the C-2/C-3 dihedral angles in this compound, but the results clearly indicate a considerable distortion of ring A. The 3β-acetoxy-5β-methyl isomer (IVa), however, gave a poorly-resolved triplet exactly similar to that reported[19] for 3α-acetoxy-5α-cholestan-2-one. The C-2 protons are therefore equivalent in their spin-spin coupling with the 3α-proton in the compound (IVa) which must have an undistorted ring A.

TABLE 2. SUMMARY OF PRODUCTS FROM REARRANGEMENT OF EPOXIDES

Epoxide	Ketonic products (%)			Hydroxy-products	Non-polar and unsaturated products
	From: C_5-O cleavage		C_4-O cleavage		
	5-Me-4-CO	A-nor-5-CO.Me	A-nor-B-homo-6-CO		
β-Epoxy-ketone (I)	39	39	—	20[a]	—
α-Epoxy-ketone (II)	16	9	—	46[a]	25[b]
3β-Acetoxy-β-epoxide (III)	ca. 10	—	—	29[c], 10[d] } 39	8[a], 19[e] } 27
3β-Acetoxy-α-epoxide (IV)	10–13	—	21–26	28[c], 9[f] } 37	8[e]
3α-Acetoxy-β-epoxide (V)	22–28			40[g], 12 } 52	6–13[a]
3α-Acetoxy-α-epoxide (VI)	—	—	—	ca. 90[c]	—

[a] Unidentified gum
[b] 4,6-Dien-3-one
[c] Unidentified crystalline compound
[d] Fluorohydrin
[e] Enol acetate
[f] 4,5-Diol
[g] Recovered epoxide, probably derived from fluorohydrin

[20] K. M. Wellman and F. G. Bordwell, *Tetrahedron Letters* No. 25, 1703 (1963).
[21] J. M. Coxon, M. P. Hartshorn and D. N. Kirk, following paper; S. Lieberman and D. K. Fukushima, *J. Amer. Chem. Soc.* **72**, 5211 (1950).

DISCUSSION

The fluorohydrin (IIIc) and the 4,5-diols (IVc and Va) are obtained from brief reaction of the corresponding 3-acetoxy-epoxides with boron trifluoride, followed by hydrolysis of the reaction mixtures, indicating that boron trifluoride coordinates rapidly with the epoxide oxygen atom in these compounds. In contrast, the epoxy-ketones are recoverable in high yield when the initially formed complexes are hydrolysed, suggesting that in these compounds boron trifluoride coordinates with the carbonyl oxygen atom in preference to the epoxide. The consequent enhancement of the —I effect of the keto-group would explain the slow rate of the subsequent rearrangement of these epoxides.

It seems probable that some of the products isolated from the more prolonged reactions are not primary products of epoxide rearrangement processes. Ketonic products were not found in appreciable amounts after short reaction times and probably arise, at least in part, from unstable fluorohydrins which are formed initially. Although this is contrary to the view expressed by Goldsmith,[5] it is supported by observations we have made on other similar systems.[22] An increase in non-polar fractions with time was noted in certain cases, indicating that some of the primary products are unstable under the reaction conditions, and undergo further reactions with loss of oxygen functions. Henbest[1b] has reported similar observations.

The experimental results described above, and summarized in Table 2, show clearly that the reactions between these epoxides and boron trifluoride are remarkably sensitive to stereochemical and vicinal effects. Few generalizations, if any, can be made on the basis of the products obtained. The observed results cannot be explained fully in terms of the factors known to influence the behaviour of trisubstituted steroidal epoxides. For example, the formation of the 3,5-diaxial compounds 3α-acetoxy-5α-methyl- (Va) and 3β-acetoxy-5β-methylcholestan-4-one (IVa) in yields greater than the less strained 3β-acetoxy-5α-methyl- isomer (IIIb) was unexpected. Reactions leading to ketonic products seem to be rather unfavourable, and this may be attributed to the difficulty of cleavage of an epoxide C—O bond in opposition to the —I effect of the C-3 substituent. The reason for the exception in the case of the β-epoxy-ketone is not clear.

The difficulty of ketone formation apparently enforces alternative reactions, notably those of fluorohydrin formation and elimination, which can proceed through intermediates having less ionic character. A similar situation has been noted[1a] for 5α,6α-epoxy cholestane. The limited number of established structures of non-ketonic products in the present series of reactions increases the difficulty of interpreting the results. It is hoped that work currently in progress in this laboratory will help to clarify the complex reactions of these and other epoxides with boron trifluoride.

EXPERIMENTAL

Epoxide rearrangements were carried out in anhydrous benzene, using freshly redistilled boron trifluoride diethyl etherate.

Rotations were measured for chloroform solutions at room temp. IR spectra were recorded for CS_2 solutions, and UV spectra for methanol solutions. Alumina used for chromatography was Peter Spence, Grade H, deactivated by the addition of 5% of 10% acetic acid. Silica gel was J. Crosfield & Sons. Light petroleum refers to the fraction of b.p. 50–70°. O.R.D. curves (in methanol) were kindly determined by Prof. W. Klyne.

[22] J. W. Blunt, M. P. Hartshorn and D. N. Kirk—to be published.

Rearrangement of 4β,5-*epoxy*-4α-*methyl*-5β-*cholestan*-3-*one* (I)

(a) *Short reaction.* A solution of the epoxy-ketone (40 mg) in benzene (1 ml) was treated with boron trifluoride etherate (0·04 ml). A colourless gel formed, and was decomposed after 10 min with sat. $NaHCO_3$ aq. Extraction with ether afforded unchanged epoxy-ketone (33 mg), m.p. and m.m.p. 92–93°, after crystallization from methanol.

(b) *Long reaction.* A solution of the epoxy-ketone (980 mg) in benzene (13 ml) was treated with boron trifluoride etherate (1 ml). After 5½ hr, when the initial gel had turned to a pale yellow-brown emulsion, the mixture was worked up with sodium acetate solution and ether, and the products were adsorbed onto a silica gel column (100 g) from light petroleum. Graded elution gave 69 fractions.

Elution with light petroleum–benzene (5:1; fractions 1–19) gave 5α-*methylcholestane*-3,4-*dione* (390 mg) as an amorphous solid, m.p. 125–128° (dec), $[\alpha]_D$ +24° (*c* 1·26), ν_{max} 3448 (OH), 1684 and 1672 cm^{-1}(α-diketone); λ_{max} 268 mμ (ε5030), O.R.D. $[\phi]_{500}$ −50°, $[\phi]_{332\cdot5}$ −600°, $[\phi]_{300}$ +1450°!

Fractions 31–50 (light petroleum–benzene, 100:3 and 2:1) gave 5β-*acetyl*-A-*norcholestan*-3-*one* (231 mg) which crystallized from methanol as prisms, m.p. 111–112°, $[\alpha]_D$ +98° (*c* 0·93), ν_{max} 1751 (5-membered ring ketone), 1692 and 1355 cm^{-1} (acetyl group), O.R.D. $[\alpha]_{500}$ +850°, $[\phi]_{307\cdot5}$ +9400°, $[\phi]_{370}$ −4950°, $[\phi]_{355}$ −4400° (Found: C, 81·4; H, 11·1. $C_{28}H_{46}O_2$ requires: C, 81·1; H, 11·3%). Rechromatography of fractions 20–30 and combined residues gave an additional 154 mg of the 5β-acetyl compound.

The remaining material, eluted by light petroleum–benzene (5:3) was an oil, ν_{max} 3460 (OH) and 1706 cm^{-1} (C:O) (Found: F, 2·1%)

3-*Acetoxy*-5-*methyl*-5α-*cholest*-2-*en*-4-*one* (Ib)

5α-Methycholestane-3,4-dione (124 mg) in acetic anhydride (0·25 ml) and pyridine (2 ml) was kept at 20° for 24 hr. The *enol acetate*, isolated by use of ether, formed needles, m.p. 141·5–142° (from methanol), $[\alpha]_D$ +31° (*c* 0·05), λ_{max} 240 mμ (ε 5160), ν_{max} 1779, 1206, and 1193 (enol acetate), 1706 cm^{-1} (C:C.C:O), O.R.D. $[\phi]_{400}$ +50°, $[\phi]_{350}$ −920°, $[\phi]_{310}$ +2950°! (Found: C, 78·7; H, 10·6. $C_{30}H_{48}O_3$ requires: C, 78·9; H, 10·6%).

Rearrangement of 4α,5-*epoxy*-4β-*methylcholestan*-3-*one* (II)

(a) *Short reaction.* This was carried out as for the β-epoxyketone above, and again led to recovery of epoxyketone, m.p. and m.m.p. 125–126° (35 mg).

(b) *Long reaction.* A solution of the α-epoxyketone (500 mg) in benzene (6·25 ml) was treated with boron trifluoride etherate (0·5 ml) for 5·5 hr. The pale brown solution was poured into sodium acetate solution and the products isolated by use of ether. Chromatography on alumina (50 g) gave the following products:-

5α-*Acetyl*-A-*norcholestan*-3-*one* (44 mg), eluted by light petroleum–benzene, crystallized from methanol in plates, m.p. 161–161·5°, $[\alpha]_D$ +209° (*c* 0·56), ν_{max} 1748 (5-membered ring ketone), 1706 and 1353 cm^{-1} (-$CO.CH_3$); O.R.D. $[\phi]_{500}$ +2750°, $[\phi]_{350}$ +40,400°, $[\phi]_{310}$ −30,300°, $[\phi]_{290}$ −5300° (Found: C, 80·8; H, 11·15. $C_{28}H_{46}O_2$ requires: C, 81·1; H, 11·3%).

4-*Methylcholesta*-4,6-*dien*-3-*one* (125 mg), eluted by the same solvent, was an oil, $[\alpha]_D$ +65° (*c* 0·98), λ_{max} 291 mμ (ε 12,300), ν_{max} 1661 cm^{-1}.

A series of oily fractions eluted by light petroleum–benzene (1:1), were mixtures of hydroxy-compounds (230 mg total), ν_{max} 3460 cm^{-1}.

5-*Methyl*-5β-*cholestane*-3,4-*dione* (80 mg) was eluted finally, by ether–acetic acid. It solidified on standing but could not be crystallized from a solvent. The solid exhibited λ_{max} 230 (ε 1470) and 260 mμ (ε 2170); ν_{max} 3571 and 3471 (OH), 1721 and 1695 cm^{-1} (α-diketone).

A similar reaction product chromatographed on silica gel gave the same compounds, but the 3,4-dione was eluted first.

Enol acetate of 5-*methyl*-5β-*cholestane*-3,4-*dione.* The dione (50 mg) in acetic anhydride (0·04 ml) and pyridine (0·4 ml) was kept at 20° for 24 hr. Isolation of the product by means of ether, and crystallization from methanol, gave the *enol acetate* (54 mg) as needles, m.p. 139–140°, $[\alpha]_D$ +61° (*c* 0·36); λ_{max} 231 mμ (ε 5160), ν_{max} 1779, 1209, and 1193 (enol acetate), 1695 cm^{-1} (C:C.C:O). (Found: C, 79·1; H, 10·55. $C_{30}H_{46}O_3$ requires: C, 78·9; H, 10·6%).

4-Methylcholesta-4,6-dien-3-one. A solution of 4-methylcholest-4-en-3-one (200 mg), chloranil (134 mg), and 65% perchloric acid (0·02 ml) in dioxan (4 ml) was heated under reflux for 2 hr. The deep brown solution was poured into 5% KOH aq and the product extracted by use of ether. The 4,6-dienone was obtained as an oil, $[\alpha]_D$ +64° (*c* 0·88), λ_{max} 291 mμ (ε 13,800), ν_{max} 1661 cm^{-1}. The IR spectrum was identical with that of the sample prepared from the α-epoxyketone (above).

The *2,4-dinitrophenylhydrazones* prepared from the two samples of 4,6-dienone were identical. The derivative crystallized from ethanol–chloroform in red needles m.p. 259–261°, λ_{max} 407 (ε 36,800), 314 (ε 16,200), 305 (ε 14,500) and 266 mμ (ε 16,500). (Found: N, 9·5. $C_{34}H_{46}O_4N_4$ requires: N, 9·5%).

Rearrangement of 3β-acetoxy-4β,5-epoxy-4α-methyl-5β-cholestane (III)

(a) *Short reaction.* A solution of the epoxy-compound (500 mg) in benzene (15 ml) was treated with boron trifluoride etherate (0·5 ml). The mixture became turbid, and began to turn pink after a few min. After 10 min 5% sodium acetate solution was added, and the product was isolated by means of ether. Trituration with pentane gave crystals (125 mg) m.p. 215–216°, which were recrystallized (acetone) to give *3β-acetoxy-5α-fluoro-4α-methylcholestan-4β-ol* (IIIc), m.p. 222–223·5°, $[\alpha]_D$ +63° (*c* 0·64), ν_{max} 3616, 1745, and 1231 cm^{-1}. (Found: C, 75·1; H, 10·9; F, 3·9. $C_{30}H_{51}FO_3$ requires: C, 75·25; H, 10·7; F, 4·0%).

Chromatography of the residues on alumina gave small quantities of products identical with those described below from a 20 min reaction, and a further quantity (65 mg) of the fluorohydrin (IIIc), m.p. 222–223°.

(b) *Long reaction.* A solution of the epoxide (1 g) in benzene (20 ml) and boron trifluoride etherate (1 ml) was allowed to stand for 20 min until it was deep purple, and was then poured into 5% sodium acetate solution and the products isolated with the use of ether. The resulting gum was adsorbed onto deactivated alumina (70 g).

Elution with light petroleum gave first a yellow gum (78 mg) showing only acetate absorption in the IR. Further elution with light petroleum gave 3-acetoxy-4-methylcholesta-3,5-diene (162 mg) which crystallized from methanol as prisms, m.p. 111–112°, $[\alpha]_D$ −93° (*c* 0·70), λ_{max} 236 mμ (ε 18,300), ν_{max} 1761 and 1215 cm^{-1} (enol acetate). (Found: C, 82·25; H, 11·1. Calc. for $C_{30}H_{48}O_2$: C, 81·8; H, 11·0%). (lit.[13] m.p. 114–116°, $[\alpha]_D$ −102°, λ_{max} 236 mμ (ε 22,400)).

4-Methylcholest-4-en-3-one (28 mg) was eluted by light petroleum–benzene (7:1), and continued elution with this solvent gave a crystalline material (204 mg), m.p. 132–146°, showing IR absorption bands ("Infracord") due to hydroxy-, acetoxy-, and keto-groups. Rechromatography failed to resolve this material into its components, but fractional crystallization from methanol, with hand-picking of crystals, ultimately gave *3β-acetoxy-5α-methylcholestan-4-one* (22 mg) as blades, m.p. 155–156°, $[\alpha]_D$ +1·5° (*c* 0·54), ν_{max} 1761, 1736, and 1231 cm^{-1} (α-acetoxy ketone); O.R.D. $[\phi]_{400}$ +36° $[\phi]_{307}$ −1410°, $[\phi]_{264}$ +2860° (infl), $[\phi]_{245}$ +2960°. (Found C, 78·75; H, 11·0. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

The more soluble fractions from the above crystallization gave an *acetoxy-alcohol* (35 mg) as needles, m.p. 135–137°, $[\alpha]_D$ +27° (*c* 0·58) ν_{max} 3584, 1733 and 1241 cm^{-1} (Found: C, 79·0; H, 11·1. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

The later fractions eluted by light petroleum–benzene (7:1) afforded the fluorohydrin (IIIc) (102 mg; m.p. 194–206°) which crystallized from acetone to give the pure compound, m.p. 222–223°.

Elution with benzene and benzene–ether (20:1) gave an acetoxy-alcohol (195 mg) which formed solvated crystals m.p. 108–110° (from methanol), m.p. 118–121° (dried at 100°/1 mm), $[\alpha]_D$ +49° (*c* 0·43), ν_{max} 3610, 1740, and 1237 cm^{-1}. (Found: C, 77·7; H, 11·2. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

Alkaline hydrolysis of the fluorohydrin (IIIc)

(a) The fluorohydrin (70 mg) was heated under reflux in 5% methanolic KOH for 4 hr. Water was added, and the product was isolated by the use of ether. The resulting gum was treated with acetic anhydride (0·3 ml) in pyridine (1 ml) at room temp overnight, and the product was again isolated by means of ether. The acetylated material, in light petroleum–benzene (20:1) was percolated through deactivated alumina (0·5 g). Evaporation of the solvent and crystallization of the residue from methanol gave 3β-acetoxy-4β,5-epoxy-4α-methyl-5β-cholestane, m.p. and m.m.p. 83–84°.

(b) The fluorohydrin (50 mg) was treated with KOH (50 mg) in 90% methanol (2 ml) at 20° for 24 hr. Dilution with water gave crude 5α-fluoro-3β,4β-diol, m.p. 182–184°, which was dissolved in methanol (10 ml) and treated with sodium metaperiodate (50 mg) in water (2 ml) for 24 hr. The product (IIId) isolated by use of ether, was a gum, ν_{max} 2728, 1730 (CHO[23]) 1715 and 1352 cm^{-1} (COMe).

Rearrangement of 3β-*acetoxy*-4α,5-*epoxy*-4β-*methyl*-5α-*cholestane* (IV)

(a) *Short reaction.* The epoxide (0·5 g) in benzene (5 ml) was treated with boron trifluoride etherate (0·5 ml). The resulting colourless gel was decomposed after 2 min by the addition of 2% $NaHCO_3$ aq, and the product was isolated by use of ether. Chromatography on alumina (25 g) gave first the unreacted epoxide (147 mg), m.p. 134–135°, eluted by light petroleum–benzene (7:1). An amorphous hydroxy-acetate (110 mg) eluted by benzene, was a powder, m.p. 199–202°, $[\alpha]_D$ +31° (*c* 0·88), ν_{max} 3590, 1740 and 1235 cm^{-1}. (Found: C, 75·2; H, 11·1. $C_{30}H_{52}O_4$ requires: C, 75·6; H, 11·0%). Finally, elution with ether gave 3β-acetoxy-4α-methyl-5α-cholestane-4β,5α-diol (130 mg), m.p. 185–186·5° (needles from methanol), $[\alpha]_D$ +37° (*c* 0·52), ν_{max} 3610, 3490, 1745 and 1237 cm^{-1}. (Found: C, 75·8; H, 11·3 Calc. for $C_{30}H_{52}O_4$: C, 75·6; H, 11·0%). (lit.[7]: m.p. 188–189°, $[\alpha]_D$ +40°).

(b) *Long reaction.* When a solution of the epoxide (2 g) in benzene (20 ml) was treated with boron trifluoride etherate (2 ml) for 25 min the gel dissolved to give a deep purple solution. The product, isolated as above, was a gum. It was adsorbed onto deactivated alumina (170 g) and eluted as follows:

Light petroleum–benzene (19:1) gave a compound (168 mg) of unknown structure. Crystallization from methanol–pentane gave soft needles, m.p. 124–126°, $[\alpha]_D$ +52° (*c* 0·53, dioxan), ν_{max} 1733, 1239 cm^{-1} (OAc).

Elution with light petroleum–benzene (5:1) gave fractions (210 mg) which were crystallized from methanol to give 3β-*acetoxy*-5-*methyl*-5β-*cholestan*-4-*one* as needles, m.p.135–137°, $[\alpha]_D$ −32° (*c* 0·3), ν_{max} 1761 and 1736 (α-acetoxy-ketone), 1239 cm^{-1} (OAc). O.R.D. $[\phi]_{400}$ −435, $[\phi]_{336}$ −4560°, $[\phi]_{286}$ +7870°, $[\phi]_{315}$ +8150° (Found: C, 78·9; H, 11·2. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

Continued elution with the same solvent and with light petroleum–benzene (4:1) gave 3β-*acetoxy*-5-*methyl*-A-*nor*-B-*homo*-5β-*cholestan*-6-*one* (515 mg), which crystallized from methanol as prisms, m.p. 93–94°, $[\alpha]_D$ +44° (*c* 0·87), ν_{max} 1748 and 1242 (OAc), 1701 cm^{-1} (7-membered ring ketone). O.R.D. $[\phi]_{500}$ +75°, $[\phi]_{315}$ +1220°, $[\phi]_{270}$ −230°, $[\phi]_{265}$ 0°. (Found: C, 78·1; H, 10·8. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

A trace (23 mg) of a crystalline acetoxy-alcohol was eluted by light petroleum–benzene (1:1). It had m.p. 146–148°, $[\alpha]_D$ −23° (*c* 0·5), ν_{max} 3580, 1740, and 1242 cm^{-1}.

Benzene–ether (20:1) gave the next major product, which was an unidentified *acetoxy-alcohol* (534 mg). It separated from aqueous methanol in fibrous crystals, m.p. 103–103·5°, $[\alpha]_D$ +41° (*c* 0·90), ν_{max} 3610, 3521 (OH), 1742 and 1238^{-1} (OAc). (Found: C, 78·3; H, 11·1. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

The final fractions, eluted by ether, gave 3β-acetoxy-4α-methyl-cholestane-4β,5α-diol, (176 mg), m.p. 185–186°.

3β-*Hydroxy*-5-*methyl*-A-*nor*-B-*homo*-5β-*cholestan*-6-*one*

3β-Acetoxy-5-methyl-A-nor-B-homo-5β-cholestan-6-one (236 mg) and KOH (100 mg) in 96% methanol (10 ml) were left for 52 hr at room temp. Addition of water caused crystallization of the 3β-*hydroxy-compound* which was recrystallized from pentane or aqueous methanol to give fibrous needles, m.p. 117–118·5°, $[\alpha]_D$ +52° (*c* 0·73), ν_{max} 3570 (OH) and 1684 cm^{-1} (7-membered ring ketone). (Found: C, 80·9; H, 11·9. $C_{28}H_{46}O_2$ requires: C, 80·7; H, 11·6%).

5-*Methyl*-A-*nor*-B-*homo*-5β-*cholestane*-3,6-*dione* (IVd)

The above 3β-hydroxy-compound (60 mg) in acetone (5 ml) was oxidized with chromic acid–sulphuric acid. Immediate dilution with water caused crystallization of the 3,6-*dione* which was

[23] D. F. Eggers and W. E. Lingren, *Analyt. Chem.* **28**, 1328 (1956).

recrystallized from methanol and gave prisms, m.p. 77–78°, $[\alpha]_D$ +37° (*c* 0·8), ν_{max} 1758 (5-membered ring ketone) and 1696 cm^{-1} (7-membered ring ketone). (Found: C, 80·8; H, 11·1. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·3%).

Hydrolysis of the acetoxy-alcohol (m.p. 103–103·5°) obtained from the 3β-acetoxy-α-epoxide

The acetoxy-alcohol (94 mg) and KOH (500 mg) in 90% methanol (10 ml) were left at 20°. Some crystals appeared slowly, and after 4 days water was added, and the solids were purified by crystallization from aqueous methanol. The *diol* formed solvated needles, m.p. 115–116°. (Found: C, 74·6; H, 11·4. $C_{28}H_{48}O_2.2H_2O$ requires: C, 74·4; H, 11·5%).

Oxidation of the diol (40 mg) with chromic acid–acetone gave a *hydroxy-ketone*, m.p. 145–146° (needles from methanol) $[\alpha]_D$ −2° (*c* 0·60), ν_{max} 3600 and 1717 cm^{-1}. (Found: C, 80·6; H, 11·3. $C_{28}H_{46}O_2$ requires: C, 81·1; H, 11·2%).

Rearrangement of 3α-acetoxy-4β, 5-epoxy-4α-methyl-5β-cholestane (V)

(a) *Short reaction.* The epoxide (70 mg) in benzene (0·7 ml) was treated with boron trifluoride etherate (0·07 ml) for 2 min. Hydrolysis with 5% sodium acetate solution, and extraction with ether gave a solid product. Trituration with pentane gave *3α-acetoxy-4α-methyl-5α-cholestane 4β,5α-diol* (25 mg), m.p. 202°–203° (needles from methanol), $[\alpha]_D$ +5° (*c* 0·93), ν_{max} 3598, 1732 cm^{-1}. (Found: C, 75·5; H, 11·25. $C_{30}H_{52}O_4$ requires: C, 75·6; H, 11·0%).

Chromatography of the residues on alumina (3 g) and elution with light petroleum–benzene (10:1) gave unchanged epoxide (28 mg), m.p. and m.m.p. 95–96°. Elution with benzene gave a product believed to be *3α-acetoxy-4α-methylcholest-5-en-4β-ol* (Vc; 12 mg), m.p. 134–136° (from methanol), $[\alpha]_D$ −46° (*c* 0·70), ν_{max}, 3610 (OH), 1739 and 1235 cm^{-1} (OAc). (Found: C, 78·2; H, 11·15. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

(b) *Long reaction.* A solution of the epoxide (533 mg) in benzene (6·4 ml) was treated with boron trifluoride etherate (0·53 ml). The solution turned bright blue, and after 1½ hr was treated with 5% sodium acetate solution. The product was isolated by use of ether. Crystallization from methanol gave *3α-acetoxy-5α-methylcholestan-4-one* (80 mg) as needles, m.p. 145–146°, $[\alpha]_D$ +45° (*c* 1·01) ν_{max} 1757 and 1727 (α-acetoxy-ketone) and 1229 cm^{-1} (OAc). O.R.D. $[\phi]_{500}$ −200°, $[\phi]_{332·5}$ +2180°, $[\phi]_{290}$ −4000°! (Found: C, 78·5; H, 10·95. $C_{30}H_{50}O_3$ requires: C, 78·55; H, 11·0%).

The remaining material was dissolved in light petroleum and adsorbed onto deactivated alumina (40 g). Elution with light petroleum gave an oil (33 mg) lacking significant spectroscopic properties.

Light petroleum–benzene (20:1) eluted the 3α-acetoxy-4β,5-epoxide (V; 211 mg) which crystallized from methanol as prisms, m.p. and m.m.p. 95–96° when mixed with the starting compound. The identity was confirmed by comparison of IR spectra.

A further quantity (75 mg) of 3α-acetoxy-5α-methylcholestan-4-one was eluted by light petroleum–benzene (4:1 and 2:1).

Finally elution with benzene and ether gave an oil (132 mg) which gave the compound believed to be the Δ^5-acetoxy alcohol (48 mg), m.p. 134–136°, on crystallization from methanol.

A reaction mixture of similar composition, employing 740 mg of the epoxide (V) was left at room temp for 5 hr, and worked up as before. The whole product was chromatographed on deactivated alumina (70 g), and gave the same products as the 1½ hr reaction, though in different proportions (see p. 2537).

Hydrolysis of the compound believed to be 3α-acetoxy-4α-methylcholest-5-en-4β-ol (Vc)

The 3α-acetoxy-compound (14 mg) in methanol (2 ml) was heated under reflux with KOH (10 mg) for ½ hr, diluted to turbidity, and cooled, giving the *3α,4β-diol* (10 mg), m.p. 203–204° (needles from methanol).

The diol (6 mg) in methanol (3 ml) was treated with sodium metaperiodate (12 mg) in water (0·2 ml) at 20° for 18 hr. Sodium metabisulphate solution was then added; and the product was isolated by use of ether, giving a gum (3·4 mg), λ_{max} 246 mμ (ε 3,600), ν_{max} 1709 and 1670 cm^{-1}.

Rearrangement of 3α-acetoxy-4α,5α-epoxy-4β-methylcholestane (VI)

A solution of the epoxide (46 mg) and boron trifluoride etherate (0·05 ml) in benzene (0·5 ml) was kept at 20° for 40 min, while a deep purple colour developed. The mixture was treated with 5%

sodium acetate solution and the product extracted by use of ether. The product was adsorbed on to deactivated alumina (4 g). Elution with light petroleum–benzene (20:1) gave an *unsaturated acetoxy-alcohol* (44 mg) which crystallized from methanol as needles (30 mg), m.p. 139–140·5°, $[\alpha]_D$ +2° (c 0·80), ν_{max} 3623 (OH), 1746 and 1239 cm^{-1} (OAc). (Found: C, 78·9; H, 10·7. $C_{30}H_{50}O_2$ requires: C, 78·55; H, 11·0%).

We thank Mr. I. R. McDonald for the determination of NMR spectra, and for many valuable discussions on their interpretation. Acknowledgement is made to the Research Committee of the New Zealand Universities Grants Committee for grants.