Steroids. Part 20.[1] Rearrangements of 5α,6α-Epoxy-10β-ethenyl- and 10β-Ethenyl-5α-hydroxy-steroids

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Homoallylic participation is not of major importance in the reactions of 5α,6α-epoxy-10β-ethenyl-steroids with boron trifluoride–ether complex, or in the sulphuric acid-catalysed rearrangement of 10β-ethenyl-5α-hydroxy-steroids to the 5β-ethenyl-Δ⁹-compounds. Deuterium substituted in the ethenyl group is not scrambled during the latter rearrangements, and the absence of cationic intermediates other than the C(10) carbocations is indicated.

HOMOALLYLIC participation in the solvolyses of sulphonate esters of 3- and 19-hydroxy-Δ⁵-steroids leads to cyclopropylmethylium ions from which the various products are derived.[2] The acid-catalysed rearrangements of 5,6-epoxy- and 5α-hydroxy-steroids proceed, at least formally, through C(5) carbocations, though the degree of rearrangement is variable (backbone- or Westphalen-type).[3] In continuation of our studies of the detailed factors which control these rearrangements,[4] and anticipating the possible intermediacy of cyclopropylmethylium ions such as (23),[5] we have examined[6] the boron trifluoride-catalysed rearrangements of the 5α,6α-epoxy-10β-ethenyl-compounds (9)—(11), and the sulphuric acid-catalysed rearrangements of the 10β-ethenyl-5α-hydroxy-compounds (28)—(31). In the epoxide reactions, homoallylic participation seems to be of minor importance since the 6β-fluoro-5α-hydroxy-compounds form a significant proportion of the products (Table 1). The 10β-ethenyl group exerts a $-I$ effect[7] which inhibits C(5)–O cleavage and allows attack of F^- at C(6) to compete effectively.[4b] Although the 10β-ethenyl-5α-hydroxy-compounds rearrange to the corresponding 5β-ethenyl-Δ⁹-compounds, the reactions appear to be relatively slow, similarly indicating ineffective homoallylic participation. From this observation, the absence of deuterium scrambling in the migrating ethenyl group, and conformational considerations, we conclude that the most likely reaction pathway for rearrangement involves no significant π-participation and no cationic intermediates before the C(10) carbocations.

Preparations and Rearrangements of the 5α,6α-Epoxides.—The hydroxy-aldehyde (1)[8] was converted into the hydroxy-diene (5) with methylenetriphenylphosphorane in dry benzene. Oxidation of the hydroxy-diene (5) with monoperphthalic acid gave the hydroxy-5α,6α-epoxide (9), which on acetylation gave the acetoxy-5α-6α-epoxide (10).[9] Reaction of the hydroxy-diene (5) with trimethyl orthoformate and perchloric acid[10] gave the methoxy-diene (6),[11] which on oxidation with monoperphthalic acid gave the methoxy-5α,6α-epoxide (11).

Reaction of a benzene solution of the acetoxy-5α,6α-epoxide (10) with boron trifluoride–ether gave a mixture from which the backbone-rearranged dimer (15) (26%) and the fluorohydrin (17) (47%) were isolated by preparative t.l.c. The yields quoted allow for the recovery of unchanged acetoxy-5α,6α-epoxide (10) (18%). The dimer (15) was identified from its 100 MHz ^{1}H n.m.r spectrum, in which the C(21)H_3 doublet (τ 9.06, *J ca.* 7 Hz) collapsed to a singlet on irradiation 147 Hz downfield.[12] Other important signals appeared at τ 2.8—4.2 (α-ethenyl 2 H), 4.5—5.4 [β-ethenyl 4 H, 2 C(3)H], and 6.66 and 6.76 [2 C(6)H]. The signal for the 13β-methyl group in the unrearranged nucleus appeared at τ 9.46. The dimeric nature of compound (15) was confirmed by an osmometric molecular weight determination [*M* 880, (14) requires 912]. The fluorohydrin (17) was readily identified by its characteristic ^{1}H n.m.r. spectrum {τ 5.7 [dm, *J ca.* 50 Hz, C(6)α-H]} and its ready conversion in methanolic potassium hydroxide into the hydroxy-5α,6α-epoxide (9).

The reaction mixture resulting from similar treatment of the hydroxy-5α,6α-epoxide (9) with boron trifluoride was difficult to separate. Acetylation followed by preparative t.l.c. allowed the isolation only of the fluorohydrin (17) (33%).

Preparative t.l.c. of the reaction mixture similarly derived from the methoxy-5α,6α-epoxide (11) gave the fluorohydrin (18) (16%), the backbone-rearranged product (19), and the ketone (20) (15%), Acetylation of a further fraction followed by preparative t.l.c. gave the Δ⁹-compound (21) (13%). The quoted yields allow for the recovery of a small quantity of the methoxy-5α, 6α-epoxide (11) (6%). The fluorohydrin (18) had characteristic spectroscopic data similar to those of the fluorohydrin (17). The backbone-rearranged compound (19) was identified from its characteristic 60 MHz ^{1}H n.m.r. spectrum[12] {τ 9.06 [d, C(21)H_3, collapsed to s on irradi-

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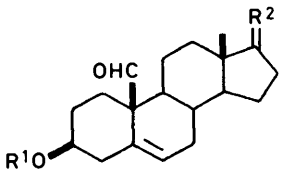
[12] J. W. Blunt, M. P. Hartshorn, and D. N. Kirk, *Tetrahedron*, 1966, **22**, 3195.



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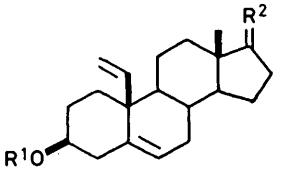

(5) R^1 = H, R^2 = β-C_8H_{17},H
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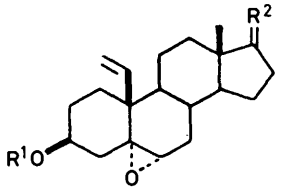
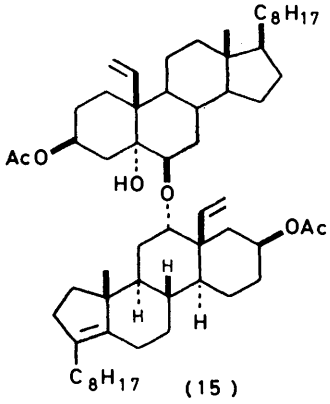


(9) R^1 = H, R^2 = β-C_8H_{17},H
(10) R^1 = Ac, R^2 = β-C_8H_{17},H
(11) R^1 = Me, R^2 = β-C_8H_{17},H
(12) R^1 = H, R^2 =
(13) R^1 = Ac, R^2 =
(14) R^1 = Me, R^2 =



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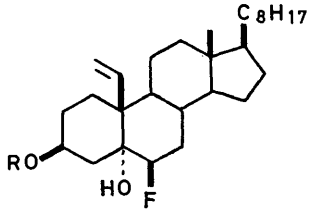

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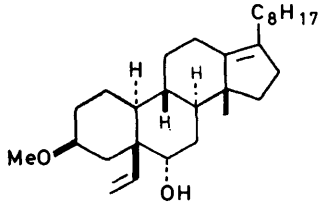
(17) R = Ac
(18) R = Me



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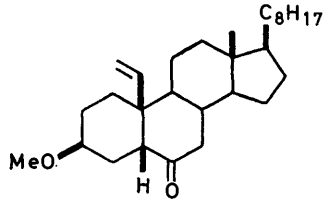

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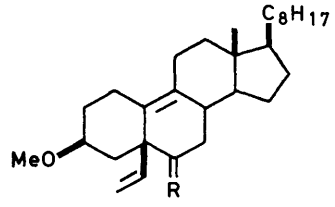
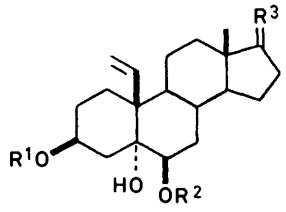
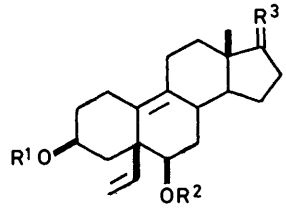


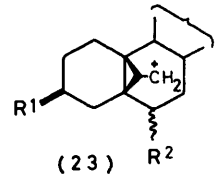
(21) R = α-OAc,H
(22) R = O



(24) R^1 = Me, R^2 = H, R^3 = β-C_8H_{17},H
(25) R^1 = Ac, R^2 = H, R^3 = O
(26) R^1 = Me, R^2 = H, R^3 = O
(27) R^1 = Ac, R^2 = H, R^3 = β-C_8H_{17},H
(28) R^1 = R^2 = Ac, R^3 = β-C_8H_{17},H
(29) R^1 = Me, R^2 = Ac, R^3 = β-C_8H_{17},H
(30) R^1 = R^2 = Ac, R^3 = O
(31) R^1 = Me, R^2 = Ac, R^3 = O



(32) R^1 = R^2 = Ac, R^3 = β-C_8H_{17},H
(33) R^1 = Me, R^2 = Ac, R^3 = β-C_8H_{17},H
(34) R^1 = R^2 = Ac, R^3 = O
(35) R^1 = Me, R^2 = Ac, R^3 = O
(36) R^1 = R^2 = H, R^3 = β-C_8H_{17},H



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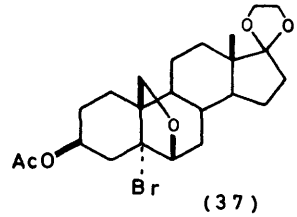


(37)

ation 88 Hz downfield] and 9.19 (s, 14β-CH_3)} and mass spectrum [13] [base peak, *m/e* 297, corresponds to loss of side chain and water from the molecular ion]. The i.r. spectrum ($\nu_{max.}$ 1 713 cm^{-1}) and ^1H n.m.r. spectrum {τ 6.58 [m, $W_{\frac{1}{2}}$ 7 Hz, C(3)H]} of the ketone (3) confirmed the presence of the carbonyl group and the 5β-configuration, respectively. The Δ^9-compound (21) showed a characteristic ^1H n.m.r. spectrum [14] [τ 9.21 (s, 13β-CH_3)], as did the ketone (22) [τ 9.22 (s, 13β-CH_3)], which was obtained from the Δ^9-compound (21) by hydrolysis and oxidation. The 5β-ethenyl group signals in the ^1H n.m.r. spectra of compounds (21) and (22) have a characteristic perturbed ABX pattern and the $W_{\frac{1}{2}}$ (*ca.* 9 Hz) of the C(3)H signal confirmed the 5β-configuration. In general, the 10β- and 5β-ethenyl groups in compounds of this series give rise to perturbed ABX patterns in the ^1H n.m.r. spectra. The perturbation increases, as expected, as the chemical shift of the proton X (4 lines, RC*H*=CH_2) approaches those of the protons A and B (8 lines, RCH=CH_2). The apparent coupling constants J_{AX} and J_{BX} are *ca.* 16—18 and 10—12 Hz and the geminal coupling constants J_{AB} are *ca.* 2—4 Hz.

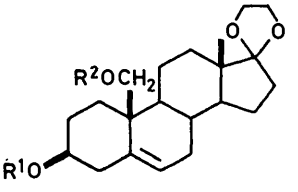
TABLE 1
Yields of fluorohydrins

Compound	(10) (3β-OAc)	(9) (3β-OH)	(11) (3β-OMe)
Yield (%)	47	33	16

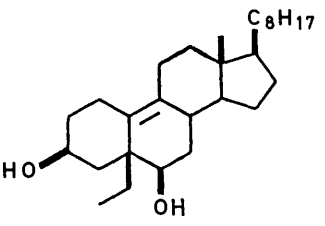
The significant yields of fluorohydrins (Table 1) in these reactions give a clear indication that homoallylic participation is relatively inefficient. The normal trend of increased C(5)–O cleavage along the series 3β-OAc, 3β-OH, 3β-OMe is observed, but significantly less C(5)–O cleavage generally occurs than in the corresponding 10β-methyl compounds.[4b] This may be ascribed to the $-I$ effect of the 10β-ethenyl group, which would destabilise the transition state leading to C(5)–O cleavage and allow attack of F^- to compete more effectively. Where C(5)–O cleavage does occur, this is assumed to lead to the C(5) carbocation from which the rearrangement products are derived.[4]

Preparation and Rearrangement of the 5α-*Hydroxy-compounds.*—Hydrolysis of the acetoxy-5α,6α-epoxide (10) [9] with aqueous periodic acid in acetone [15] gave the acetoxy-5α,6β-diol (27), which on acetylation gave the diacetoxy-5α-hydroxy-compound (28).

The hydroxy-aldehyde (3) [16] was prepared by the method of Bowers and his co-workers with one minor modification. The bromo-ether (37) was converted into the acetoxy-19-hydroxy-compound (38) by heating under reflux with zinc and ethanol adjusted to an initial pH of 5.5 with glacial acetic acid. Failure to add acetic acid resulted in formation of the diol (39), which was not readily selectively oxidised or acylated. Reaction of the hydroxy-aldehyde (3) with methylenetriphenylphosphorane gave the hydroxy-ethylenedioxy-diene (7). Selective oxidation of this with monoperphthalic acid gave the hydroxy-ethylenedioxy-epoxide (12), which was acetylated to give the acetoxy-compound (13). Hydrolysis of the compound (13) with aqueous perchloric acid in ethyl methyl ketone [17] gave the dihydroxy-ketone (25), which was acetylated without purification and gave the diacetoxy-5α-hydroxy-ketone (30).



(38) R^1 = Ac, R^2 = H
(39) R^1 = R^2 = H
(40) R^1 = R^2 = Ac
(41) R^1 = H, R^2 = Ac
(42) R^1 = Ts, R^2 = Ac
(43) R^1 = Me, R^2 = H



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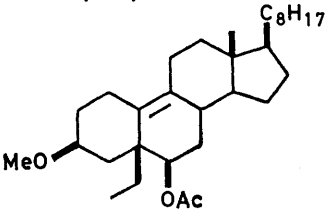

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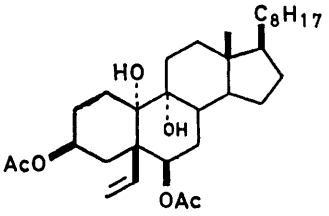

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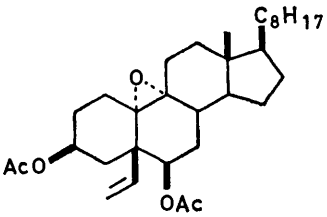

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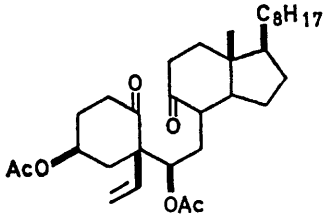


(48)

The methoxy-ethylenedioxy-aldehyde (4) which was required for preparation of a deuterium-labelled substrate (see below) was prepared from the 19-hydroxy-compound (38).* Acetylation of the latter gave the diacetate (40), which was selectively hydrolysed to the 19-acetoxy-3β-hydroxy-compound (41). Treatment of

* The more direct route from 3β-methoxyandrost-5-en-17-one is not available owing to the instability of 5α-bromo-6β-hydroxy-3β-methoxy-steroids (B. W. Cubberley and B. A. Marples, *J.C.S. Perkin I*, 1974, 9).

[13] (*a*) G. Snatzke and H. W. Fehlhaber, *Annalen*, 1964, **676**, 188; (*b*) J. W. Blunt, M. P. Hartshorn, and D. N. Kirk, *Tetrahedron Letters*, 1966, 2125.

[14] A. Fischer, M. J. Hardman, M. P. Hartshorn, D. N. Kirk, and A. R. Thawley, *Tetrahedron*, 1967, **23**, 159.

[15] L. F. Fieser and S. Rajagopalan, *J. Amer. Chem. Soc.*, 1949, **71**, 3938.

[16] O. Halpern, I. Delfin, L. Magaña, and A. Bowers, *J. Org. Chem.*, 1966, **31**, 693.

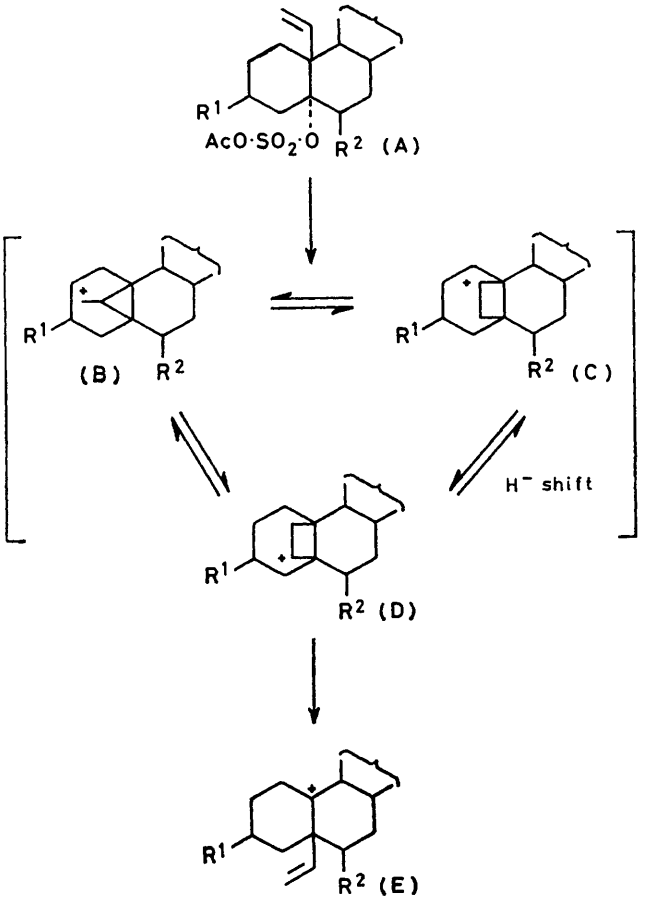
[17] J. M. Diggle, M. D. Halliday, G. D. Meakins, and M. S. Saltmarsh, *Chem. Comm.*, 1969, 819.

compound (41) with toluene-*p*-sulphonyl chloride in pyridine gave the tosylate (42), which was converted by methanolysis and basic hydrolysis into the methoxy-ethylenedioxy-19-hydroxy-compound (43). In this sequence, partial hydrolysis of the ethylenedioxy-group occurred and it was necessary to treat the crude product with ethylene glycol under the usual conditions. Oxidation of compound (43) gave the required methoxy-ethylenedioxy-aldehyde (4), which was converted into the methoxy-acetoxy-5α-hydroxy-ketone (31) as above *via* the methoxy-ethylenedioxydiene (8), the methoxy-ethylenedioxy-epoxide (14), and the dihydroxy-ketone (26).

Rearrangement of the 5α-hydroxy-compounds (28), (30), and (31) in H_2SO_4–AcOH–Ac_2O [14] gave the Δ^9-compounds (32), (34), and (35), respectively, as the major products, which were purified by t.l.c. The ^1H n.m.r. spectrum of the Δ^9-compound (32) showed a characteristic [14] signal for the 13β-methyl group (τ 9.2). The 5β-ethenyl group signals show a slightly perturbed ABX pattern in which the α-ethenyl proton appears as a quartet (τ 4.3). The remaining eight lines are superimposed on the C(3)H and the C(6)H multiplets (τ 4.6—5.5) and the apparent coupling constants are J_{trans} 16, J_{cis} 11, and J_{gem} 3 Hz. The ^1H n.m.r. spectrum of the Δ^9-diol (36), which was obtained by hydrolysis of compound (32), showed the expected signals [14] for the C(3)H [τ 6.1 (m, $W_{\frac{1}{2}}$ *ca.* 10 Hz)] and the C(6)H [τ 6.55 (m, $W_{\frac{1}{2}}$ *ca.* 16 Hz)]. Hydrogenation of the hydrolysis product (36) gave the 5β-ethyl compound (44), which had a ^1H n.m.r. spectrum similar to that of compound (45).[11] Further evidence in support of the proposed structure of compound (32) was obtained from its oxidation by osmium tetraoxide, which gave the 9,10-diol (46) and by monoperphthalic acid, which gave the epoxide (47). The 9,10-diol (46) is assigned the 9α,10α-configuration owing to the expected preferential α-attack and the high-field position (τ 9.23) of the 13β-methyl signal in the ^1H n.m.r. spectrum. A 9β-hydroxy-group would be expected to exert a considerable deshielding effect. The epoxide (47) is similarly tentatively assigned the α-configuration. Oxidation of the 9,10-diol (46) with lead tetra-acetate gave the diketone (48), further supporting the structural assignments. The ^1H n.m.r. spectra of compounds (34) and (35) were characteristic and similar to that of compound (32).

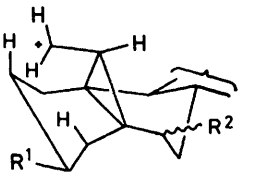
Although no quantitative data are available on the rates of reaction of the 10β-ethenyl-5α-hydroxy-compounds (28), (30), and (31), it was clear from t.l.c. of the reaction mixtures that the reactions proceeded rather more slowly than for the corresponding 10β-methyl-5α-hydroxy-compounds. As was noted for the epoxide rearrangements, homoallylic participation does not appear to be particularly important.

Preparation and Rearrangement of Deuteriated 5α-Hydroxy-compounds.—The rearrangement of a 5α-hydroxy-10β-ethenyl compound would be expected to involve the acetyl sulphate [(A), Scheme 1].[12] Homoallylic participation could in principle give the cyclopropylmethylium ion (B) and the cyclobutylium ion (C). The ion (E), from which the Δ^9-compound is derived, could be formed directly from ion (B) or (D) and the latter could be formed from (B) or (C) as indicated.

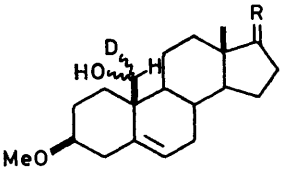


SCHEME 1

The cyclopropylmethylium ion (B) (classical or non-classical [5]) is likely to be seriously destabilised since it cannot readily take up the preferred bisected conformation (49) [5] owing to steric repulsion between one of the



(49)



(50) R = 

(51) R = β-C_8H_{17},H

methylene hydrogen atoms and the hydrogen atoms at C(2) and/or C(4).* Accordingly, the pathways (A) ⟶ (B) ⟶ (E) and (A) ⟶ (B) ⟶ (D) ⟶ (E) do not appear very favourable. The alternative pathway

* The equivalent conformation in which the methylene group is held over ring B would be similarly sterically hindered.

(A)[⟶ (B)] ⟶ (C) ⟶ (D) ⟶ (E), which involves a 1,2-shift of a hydride ion, should be detectable by using substrates deuteriated in the ethenyl group. Accordingly, we examined the rearrangements of β-deuteriated samples of the 3β,6β-diacetoxy-compound (28) and α-deuteriated samples of the 3β-methoxy-6β-acetoxy-compounds (29) and (31). Table 2 shows the deuterium contents of the starting materials and products, determined mass spectrometrically, from which it is clear that no deuterium is lost during rearrangement.

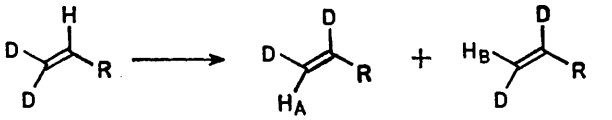
TABLE 2

Deuterium contents (%) of starting materials and products in Westphalen rearrangements

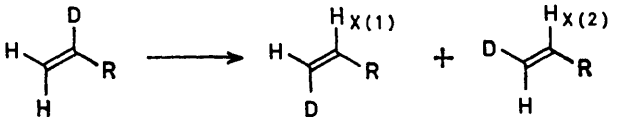
	α-Deuteriated		β-Deuteriated				Deuterium levels		
Compound	$^2H_1$	$^2H_0$		$^2H_2$	$^2H_1$	$^2H_0$	Product	$^2H_2$	$^2H_1$	$^2H_0$
(28)			(a)	50.6	38.4	11.0	(32)	(a) 53.0	37.5	9.5
			(b)	85.5	11.2	3.3		(b) 86.5	11.1	2.4
(29)	84.8	15.2					(33)		84.5	15.5
(31)	83.5	16.5					(35)		83.8	16.2

The β-deuteriated sample (28) (a) was prepared by the route outlined above employing trideuteriomethyltriphenylphosphonium iodide in the normal Wittig reaction, and the β-deuteriated sample (28) (b) was similarly prepared employing trideuteriomethyltriphenylphosphonium bromide in the modified Wittig reaction.[18] Trideuteriomethyltriphenylphosphonium iodide was prepared in the normal way from trideuteriomethyl iodide, and trideuteriomethyltriphenylphosphonium bromide was prepared from the undeuteriated quaternary salt by base-catalysed deuterium–proton exchange.[19] The partially α-deuteriated compound (29) was prepared from the methoxy-ethylenedioxy-aldehyde (4). Reduction of compound (4) with lithium aluminium deuteride gave the monodeuterio-compound (50). Oxidation, as before, gave the essentially monodeuteriated aldehyde (4) which was converted into the α-deuteriated compound (31) by the sequence of reactions already described. Similarly, the essentially monodeuteriated aldehyde (2) [11] was obtained from the monodeuterio-alcohol (51) and converted through the α-deuteriated-compounds (6),[11] (11), and (24) into the α-deuteriated 5α-hydroxy-6β-acetoxy-compound (29).

In our original studies [6] it appeared from integration of the olefinic region of the ^1H n.m.r. spectrum of the product (32) (a) that some scrambling of the deuterium had occurred. Owing to the relatively low level of deuterium content it was not possible to detect any significant change in the spin–spin coupling pattern of the olefinic multiplets. We were concerned to establish this apparent scrambling unequivocally and hence repeated the reaction using the more heavily deuteriated mixture (28) (b) and the α-deuteriated samples of compounds (29) and (31) (Table 2). We anticipated that any scrambling of the label would be more readily observed in these samples. The product (32) (b), however, showed no evidence of deuterium scrambling. The expected broadened singlets for H_A and H_B in the product (Scheme 2) were not observed. Two low intensity doublets at τ 4.7 (*J ca.* 10 Hz) and 5.06 (*J ca.* 17.5 Hz) which were detected by computer-assisted accumulation were present as a result of the small amount of monodeuteriocompound present. In support of these observations, we could detect no evidence of scrambling of label in the products (33) and (35). The anticipated low-field doublets for $H_{X(1)}$ and $H_{X(2)}$ (Scheme 3) were not observed in either product. A low intensity quartet which was detected in each case by accumulation was present, from the residual $^2H_0$ species.



SCHEME 2



SCHEME 3

We are now convinced that no significant scrambling of deuterium occurs in the 1,2-ethenyl group shift and thus the pathway (A)[⟶ (B)] ⟶ (C) ⟶ (D) ⟶ (E) (Scheme 1) is not involved in the rearrangement.

In view of the unfavourable nature of the alternative pathways (A) ⟶ (B) ⟶ (E) and (A) ⟶ (B) ⟶ (D) ⟶ (E) (see above), we conclude that in the 5α-hydroxy-compounds the migration of the ethenyl group is concerted with C(5)–O cleavage and the first formed ionic intermediate is the C(10) carbocation (E) (Scheme 1). This conclusion is supported by the relative slowness of rearrangement and is in accord with our earlier work on Westphalen-type rearrangements.[4,11]

EXPERIMENTAL

Solutions were dried over anhydrous sodium sulphate and solvents were removed *in vacuo* on a rotary evaporator. Plates (1 m × 0.5 mm thick) of Kieselgel P254 (Merck) were used for preparative t.l.c. and deactivated alumina (grade III) was used for column chromatography.

I.r. spectra were determined with Perkin-Elmer 237 and 257 spectrophotometers. ^1H N.m.r. spectra were determined for solutions in deuteriochloroform (unless specified otherwise), routinely at 60 MHz with a Perkin-Elmer R10 spectrometer, at 90 MHz with a Perkin-Elmer R32 spectrometer, and at 100 MHz with a Varian HA-100D spectro-

[18] G. W. Buchanan and A. G. Gustafson, *J. Org. Chem.*, 1973, **38**, 2910.

[19] M. Pomerantz and G. W. Gruber, *J. Amer. Chem. Soc.*, 1971, **93**, 6615.

meter. Mass spectra were recorded with A.E.I. MS 902 and MS 12 spectrometers. Rotations were measured for solutions at ambient temperature in chloroform with a Bendix polarimeter 143C. M.p.s were measured with a Kofler hot-stage apparatus.

5,6α-Epoxy-19-methylene-5α-cholestan-3β-ol (9).—A 2.0M-solution of n-butyl-lithium in hexane (26 ml) was added to a suspension of methyltriphenylphosphonium iodide (22 g) in dry benzene (200 ml), and the mixture was stirred under nitrogen for 2 h. A solution of the hydroxy-aldehyde (1)[8] (8.1 g) in dry benzene (200 ml) was added slowly. The mixture was stirred overnight at room temperature and then heated under reflux for 6 h. After cooling the mixture was poured into water and extracted with ether, and the combined extracts, after drying and evaporating, yielded an oil. Column chromatography, eluting successively with benzene and 10% ether in benzene, gave 19-methylene-cholest-5-en-3β-ol (5) (5.6 g), m.p. 112—113° (from methanol). Epoxidation of this hydroxy-diene (5) (2.2 g) with a 4-molar excess of monoperphthalic acid in ether solution overnight, gave, after the usual work-up, the *hydroxy-5α,6α-epoxide* (9) (2.35 g), a gum, $[\alpha]_D$ −55° (*c* 0.8), $\nu_{max.}$ 3 630 and 3 380 (OH), and 3 090, 1 640, and 920 cm^{-1} (CH_2=CHR), τ (CCl_4) 4.22 (m, RC*H*=CH_2), 4.75 (m, *J* 3.5 Hz, RCH=C*H*$_2$), 6.35 (m, $W_{\frac{1}{2}}$ *ca.* 25 Hz, 3-H), 6.82br (s, OH), 7.12 [d, *J* (apparent) 3.5 Hz, 6-H], and 9.49 (s, 13β-Me) (Found: C, 81.2; H, 10.95. $C_{28}H_{46}O_2$ requires C, 81.1; H, 11.2%).

3β-Acetoxy-5,6α-epoxy-19-methylene-5α-cholestane (10).—Acetylation of the hydroxy-5α,6α-epoxide (9) (2.35 g) with acetic anhydride–pyridine gave the acetoxy-5α,6α-epoxide (10) (2.1 g), m.p. 75—76° (from methanol), $[\alpha]_D$ −55° (*c* (0.83), τ (CCl_4) 4.2 (m, RC*H*=CH_2), 4.75 (m, RCH=C*H*$_2$), 5.2 (m, 3-H), 7.11 [d, *J* (apparent) 4 Hz, 6-H], 8.1 (s, OAc), and 9.48 (s, 13β-Me) (lit.,[9] m.p. 77°, $[\alpha]_D$ −53°).

5,6α-Epoxy-3β-methoxy-19-methylene-5α-cholestane (11).—A solution of the hydroxy-diene (5) (1.1 g) in trimethyl orthoformate (11 ml) was treated with perchloric acid (60% w/v; 1.1 ml)[10] and set aside at room temperature for 15 min. The mixture was poured into sodium hydrogen carbonate solution and extracted with ether. The extract was dried and evaporated to give the crude methoxy-diene (6), which was oxidised with monoperphthalic acid in ether solution, as above, to give the *methoxy-5α,6α-epoxide* (11) (1.15 g), m.p. 87—88° (from methanol), $[\alpha]_D$ −63.5° (*c* 0.77), $\nu_{max.}$ 2 830 (OMe), and 3 090 and 920 cm^{-1} (CH_2=CHR), τ (CCl_4) 4.25 (m, RC*H*=CH_2), 4.8 (m, RCH=C*H*$_2$), 6.7 (m, 3-H), 6.81 (s, OMe), 7.15 [d, *J* (apparent) 4 Hz, 6-H], and 9.49 (s, 13β-Me) (Found: C, 81.35; H, 11.4. $C_{29}H_{48}O_2$ requires C, 81.25; H, 11.3%).

Reaction of 3β-Acetoxy-5,6α-epoxy-19-methylene-5α-cholestane (10) *with Boron Trifluoride–Ether*.—A solution of the acetoxy-epoxide (10) (2.0 g) in benzene (40 ml) was treated with boron trifluoride–ether complex (2 ml), set aside for 5 min, and then poured into saturated sodium hydrogen carbonate solution. The mixture was extracted (×2) with ether and the combined extracts were washed with water and dried. Evaporation gave a crude product which on preparative t.l.c. [eluting with benzene–ethyl acetate (25 : 1)] gave the *dimeric ether* (15) (430 mg), m.p. 171—173° (from methanol), $[\alpha]_D$ +10.5° (*c* 2.1), $\nu_{max.}$ 3 610 and 3 450 (OH), 1 740 and 1 720 (C=O), 1 245 (C–O), and 3 080 and 915 cm^{-1} (CH_2=CHR), τ (100 MHz) 2.8—4.1 (m, 2 × RC*H*=CH_2), 4.5—5.4 (m, 2 × RCH=C*H*$_2$ and 2 × 3-H), 6.7 (m, 2 × 6-H), 8.0 (s, OAc), 8.09 (s, OAc), 9.06 [d, *J* 7 Hz, C(21)H_3, collapsed to s on irradiation 147 Hz downfield], 9.18 (s, 14β-Me), and 9.46 (s, 13β-Me) [Found: C, 78.3; H, 10.75%; *M* (osmometry), 882. $C_{60}H_{16}O_6$ requires C, 78.9; H, 10.6%; *M*, 912]; and a second fraction, which on further t.l.c. [eluting (×2) with benzene–ethyl acetate (40 : 1)] gave *3β-acetoxy-6β-fluoro-5-hydroxy-19-methylene-5α-cholestane* (17) (780 mg), m.p. 163—164° (from methanol), $[\alpha]_D$ +15.5° (*c* 0.75), $\nu_{max.}$ 3 610 and 3 450 (OH), 1 740 and 1 720 (C=O), 1 250 (C–O), and 3 090 and 920 cm^{-1} (CH_2=CHR), τ (CCl_4) 3.7 [q, *J* (apparent) 18 and 10 Hz, RC*H*=CH_2], 4.4—5.4 (m, 3-H and RCH=C*H*$_2$), 5.7 (dm, J_{HF} 48 Hz, 6-H), 6.6br (s, OH), 8.02 (s, OAc), and 9.41 (s, 13β-Me) (Found: C, 76.0; H, 10.6. $C_{30}H_{49}FO_3$ requires C, 76.5; H, 10.35%), and the unchanged acetoxy-5α,6α-epoxide (10) (360 mg).

Conversion of the Fluorohydrin (17) *into the Hydroxy-epoxide* (9).—A solution of the fluorohydrin (17) in methanolic potassium hydroxide (5%) was heated under reflux for 30 min and poured into water. Extraction with ether in the usual way gave the hydroxy-5α,6α-epoxide (9), identical with an authentic sample.

Reaction of 5,6α-Epoxy-3β-hydroxy-19-methylene-5α-cholestane (9) *with Boron Trifluoride–Ether*.—A solution of the hydroxy-epoxide (9) (1.0 g) in benzene (20 ml) was treated with boron trifluoride–ether complex (1 ml) and set aside for 5 min. The crude product, isolated as above, was acetylated with acetic anhydride in pyridine and gave material which on preparative t.l.c. [eluting (×4) with benzene–ethyl acetate (25 : 1)] yielded the fluorohydrin (17) (330 mg). No other identified products were isolated.

Reaction of 5,6α-Epoxy-3β-methoxy-19-methylene-5α-cholestane (11) *with Boron Trifluoride–Ether*.—A solution of the methoxy-epoxide (11) (760 mg) in benzene (15 ml) was treated with boron trifluoride–ether complex (0.75 ml) and set aside for 2 min. Preparative t.l.c. of the crude product, isolated as above [eluting with benzene–ethyl acetate (19 : 1)] gave five fractions. It was not possible to purify the most polar (230 mg) and least polar (53 mg) fractions, and these were discarded. The second most polar fraction (91 mg) was acetylated, and further preparative t.l.c. [eluting with benzene–ethyl acetate (19 : 1)] gave *6α-acetoxy-5-ethenyl-3β-methoxy-19-nor-5β-cholest-9-ene* (21) (60 mg), a gum, $[\alpha]_D$ +66° (*c* 0.52), $\nu_{max.}$ 3 070, 1 635, and 910 (CH_2=CHR), 2 820 (MeO), 1 740 (C=O), and 1 245 cm^{-1} (C–O), τ (CCl_4) 4.05 (m, RC*H*=CH_2), 4.8—5.5 (m, RCH=C*H*$_2$ and 6-H), 6.57 (m, $W_{\frac{1}{2}}$ 10 Hz, 3-H), 6.80 (s, OMe), 8.06 (s, OAc), and 9.21 (s, 13β-Me) (Found: M^+, 470.3770. Calc. for $C_{31}H_{50}O_3$: *M*, 470.3760). Preparative t.l.c. of the third most polar fraction (159 mg) [eluting with ether–petroleum (1 : 3)] gave *6β-fluoro-5-hydroxy-3β-methoxy-19-methylene-5α-cholestane* (18) (114 mg), m.p. 147—148° (from methanol, $[\alpha]_D$ +34° (*c* 2.0), $\nu_{max.}$ 3 630 and 3 450 (OH), 3 090, 1 637, and 940 (CH_2=CHR), and 2 835 cm^{-1} (OMe), τ (CCl_4) 3.75 (m, RC*H*=CH_2), 4.6—5.3 (m, RCH=C*H*$_2$), 5.6 (dm, J_{HF} 50 Hz, 6-H), 6.34 (m, $W_{\frac{1}{2}}$ 24 Hz, 3-H), 6.66 (s, OMe), and 9.42 (s, 13β-Me) (Found: C, 77.7; H, 11.0. $C_{29}H_{49}FO_2$ requires C, 77.6; H, 11.0%), and *5-ethenyl-6α-hydroxy-3β-methoxy-14-methyl-18,19-bisnor-5β,8α,9β,10α,14β-cholest-13(17)-ene* (19) (15 mg), a gum, $\nu_{max.}$ 3 630 (OH), 3 080, 1 635, and 930 (CH_2=CHR), and 2 835 cm^{-1} (OMe), τ (CCl_4) 3.7 (m, RC*H*=CH_2), 4.8—5.3 (m, RCH=C*H*$_2$), 6.25 (m, $W_{\frac{1}{2}}$ 8 Hz, 6-H), 6.61 (m, $W_{\frac{1}{2}}$ 9 Hz, 3-H), 6.94 (s, OMe), and 9.06 [d, C(21)H_3, collapsed to s on irradiation 88 Hz downfield] (Found: M^+, 428.3648. Calc. for $C_{29}H_{48}O_2$: *M*, 428.3654). Further preparative t.l.c. of the fourth most polar fraction (172 mg) [eluting with ether–petroleum (1 : 3)] gave *3β-methoxy-19-methylene-5β-cholestan-6-one* (20) (107 mg), a

gum, $[\alpha]_D$ −37° (*c* 1.7), $\nu_{max.}$ 3 100, 1 640, and 925 (CH_2=CHR), 2 835 (OMe), and 1 713 cm^{-1} (C=O), τ (CCl_4) 4.16 (m, RC*H*=CH_2), 4.73—5.27 (m, RCH=CH_2), 6.58 (m, $W_{\frac{1}{2}}$ 7 Hz, 3-H), 6.77 (s, OMe), and 9.39 (s, 13β-Me) (Found: C, 81.2; H, 11.0. $C_{29}H_{48}O_2$ requires C, 81.25; H, 11.3%), and the methoxy-5α,6α-epoxide (42 mg).

5-Ethenyl-3β-methoxy-19-nor-5β-cholest-9-en-6-one (22).—The Δ⁹-compound (21) (27 mg) was hydrolysed by heating under reflux in aqueous methanolic potassium hydroxide (5%). Dilution with water and extraction with ether in the usual way gave the crude alcohol, which was taken up in acetone and treated with an excess of Jones reagent at 0 °C for 5 min. The mixture was poured into water, and extracted with ether (×2). The combined extracts were washed with sodium hydrogen carbonate solution and water and dried. Removal of the solvent and preparative t.l.c. of the residue gave the ketone (2) (10 mg), m.p. 69—71° (from methanol), $\nu_{max.}$ 2 830 (OMe), 1 718 (C=O), and 935 cm^{-1} (CH_2=CHR), τ (100 MHz) 4.15 (m, RC*H*=CH_2), 4.84—5.16 (m, RCH=CH_2), 6.50 (m, $W_{\frac{1}{2}}$ 8.5 Hz, 3-H), 6.71 (s, OMe), and 9.22 (s, 13β-Me) (Found: M^+, 426.3502. Calc. for $C_{29}H_{46}O_2$: *M*, 426.3498).

3β-Acetoxy-19-methylene-5α-cholestane-5,6β-diol (27).—A solution of the acetoxy-5α,6α-epoxide (10) [9] (250 mg) and periodic acid dihydrate (150 mg) in aqueous acetone was heated under reflux for 30 min. Water was added to precipitate the diol (27) (200 mg), m.p. 199—200° (from methanol), $[\alpha]_D$ +8° (*c* 0.25) (Found: M^+, 474.3695. Calc. for $C_{30}H_{50}O_4$: *M*, 474.3709).

3β,6β-Diacetoxy-19-methylene-5α-cholestan-5-ol (28).—Acetylation of the diol (27) (200 mg) with an excess of acetic anhydride in pyridine at room temperature overnight gave the diacetate (28) (200 mg), a gum, $[\alpha]_D$ −24° (*c* 0.2), τ (CCl_4) 3.55 (m, RC*H*=CH_2), 4.5—5.3 (m, RCH=CH_2 and 3- and 6-H), 7.95 (s, OAc), 8.08 (s, OAc), and 9.42 (s, 18-Me) [Found: *m/e*, 456.3597. Calc. for *M* ($C_{39}H_{52}O_5$) − AcOH: *m/e*, 456.3603].

17,17-Ethylenedioxy-19-methyleneandrost-5-en-3β-ol (7).—A 2.6M-solution of n-butyl-lithium in hexane (7.5 ml) was added, under nitrogen, to a suspension of freshly prepared methyltriphenylphosphonium iodide (7.8 g) in dry benzene (250 ml). The mixture was stirred, at room temperature, for 2 h and the hydroxy-aldehyde (3)[16] (2.5 g), in dry benzene (100 ml), was added, dropwise, over 1 h. The mixture was stirred overnight, then heated under reflux for 4 h. After dilution with water and work-up, as before, the product was chromatographed on silica gel and gave [eluting with ethyl acetate–benzene (1 : 5)] the *hydroxy-ethylenedioxy-diene* (7) (1.9 g), m.p. 149—150° (from methanol), $[\alpha]_D$ +58° (*c* 1.5), $\nu_{max.}$ 3 460 cm^{-1} (OH), τ 4.0—4.5 (m, RC*H*=CH_2 and 6-H), 4.6—5.3 (m, RCH=CH_2), 6.12 (s, O·CH_2·CH_2·O), 6.5 (m, 3-H), and 9.2 (s, 13-Me) (Found: C, 76.4; H, 9.7. $C_{22}H_{32}O_3$ requires C, 76.7; H, 9.35%).

5,6α-Epoxy-17,17-ethylenedioxy-19-methylene-5α-androstan-3β-ol (12).—A solution of the hydroxy-ethylenedioxy-diene (7) (1.1 g) in ether (100 ml) was treated with an excess of monoperphthalic acid in ether in the usual manner and gave the crude 5α,6α-epoxide (12) (1.1 g), the bulk of which was used without purification. Crystallisation of a sample from dichloromethane–ether–petroleum gave pure *5α,6α-epoxide* (12), m.p. 132—133°, $[\alpha]_D$ −100.2° (*c* 0.82), $\nu_{max.}$ 3 460 cm^{-1} (OH), τ 4.0—4.46 (m, RC*H*=CH_2), 4.46—5.15 (m, RCH=CH_2), 6.18 (s, −O−CH_2−CH_2−O−), 6.0—6.5 (m, 3-H), 7.0 (d, *J* 4 Hz, 6-H), and 9.29 (s, 13-Me) (Found: C, 73.0; H, 9.0. $C_{22}H_{32}O_4$ requires C, 73.3; H, 8.95%).

3β-Acetoxy-5,6α-epoxy-17,17-ethylenedioxy-19-methylene-5α-androstane (13).—Acetylation of the crude epoxide (12) (800 mg) with acetic anhydride in pyridine gave the acetoxy-5α,6α-epoxide (13) (800 mg), m.p. 135—136° (from methanol), $[\alpha]_D$ −101° (*c* 1.0), $\nu_{max.}$ 1 735 (C=O) and 1 250 cm^{-1} (C−O), τ 3.9—4.4 (m, RC*H*=CH_2), 4.4—5.4 (m, RCH=CH_2 and 3-H), 6.13 (s, −O−CH_2−CH_2−O−), 7.0 (d, 6-H), 8.03 (s, OAc), and 9.3 (s, 13-Me) (Found: M^+, 402.2404. Calc. for $C_{24}H_{34}O_5$: *M*, 402.2406).

3β,6β-Diacetoxy-5-hydroxy-19-methylene-5α-androstan-17-one (30).—A solution of the epoxy-acetate (13) (800 mg) and aqueous perchloric acid (60%; 0.5 ml) in ethyl methyl ketone (25 ml) was set aside at room temperature for 15 min. The solution was diluted with ether, washed with aqueous sodium hydrogen carbonate solution, and dried. Removal of the solvent gave the crude diol (25) (800 mg). Acetylation of the diol (25) (600 mg) with acetic anhydride (1.4 ml) in pyridine (3 ml) on a boiling water-bath for 2 h, followed by the usual work-up and preparative t.l.c. {eluting with ether (×2)} gave the diacetate (30) (400 mg), m.p. 108—109° (from dichloromethane–petroleum), $[\alpha]_D$ +25° (*c* 6.0), $\nu_{max.}$ 3 490 (OH), 1 740 and 1 720 (C=O), and 1 250 cm^{-1} (C−O), τ 3.5 (m, RC*H*=CH_2), 4.45—5.25 (m, RCH=CH_2, 3- and 6-H), 7.3br (s, OH), 7.9 (s, OAc), 8.02 (s, OAc), and 9.21 (s, 13-Me) (Found: M^+, 418.2332. Calc. for $C_{24}H_{34}O_6$: *M*, 418.2355).

3β,19-Diacetoxy-17-17-ethylenedioxyandrost-5-ene (40).—A solution of the hydroxy-acetate (38)[16] (10 g) in pyridine (30 ml) and acetic anhydride (14 ml) was heated on a boiling water-bath for 2 h. The usual work-up afforded the *diacetate* (40) (10 g), m.p. 102—104° (from methanol), $[\alpha]_D$ −99.5° (*c* 1.1), $\nu_{max.}$ 1 735 (C=O) and 1 250 cm^{-1} (C−O), τ 4.3—4.5 (m, 6-H), 5.8 (q, *J* 12 Hz, 19-H_2), 6.15 (s, −O−CH_2−CH_2−O−), 7.98 (s, OAc), 8.0 (s, OAc), and 9.12 (s, 13-Me) (Found: C, 69.95; H, 8.7%; *m/e*, 372.2308. $C_{25}H_{36}O_6$ requires C, 69.4; H, 8.4%; *M* − AcOH, 372.2301).

19-Acetoxy-17,17-ethoxylenedioxyandrost-5-en-3β-ol (41).—Anhydrous sodium carbonate (5 g) was added to a methanolic solution of the diacetate (40) (10 g in 150 ml) and the suspension was stirred overnight at room temperature. After dilution with water, the solution was extracted with chloroform (×2) and the combined extracts were dried and evaporated to give the *hydroxy-acetate* (41) (6 g), m.p. 95—97° (from aqueous acetone), $[\alpha]_D$ −118.5° (*c* 0.95), $\nu_{max.}$ 3 480 (OH), 1 735 (C=O), and 1 240 cm^{-1} (C−O), τ 4.3—4.55 (m, 6-H), 5.8 (q, *J* 12 Hz, 19-H_2), 6.15 (s, −O−CH_2−CH_2−O−), 6.0—6.6 (m, 3-H), 7.98 (s, OAc), and 9.13 (s, 13-Me) (Found: C, 70.9; H, 9.0. $C_{23}H_{34}O_5$ requires C, 70.75; H, 8.8%).

17,17-Ethylenedioxy-3β-methoxyandrost-5-en-19-ol (43).—A solution of the hydroxy-acetate (41) (5 g) and toluene-*p*-sulphonyl chloride (20 g) in pyridine was set aside at room temperature overnight. The usual work-up gave the tosylate (42) (5 g), $\nu_{max.}$ 1 735 (C=O), 1 250 (C−O), 1 360, and 1 175 cm^{-1} (RSO_2·O), τ 2.15—2.75 (m, aromatic H_4), 4.35—4.55 (m, 6-H), 5.83 (q, 19-H_2), 6.13 (s, −O−CH_2−CH_2−O−), 6.0—6.25 (m, 3-H), 7.58 (s, *Me*C_6H_4), 8.0 (s, OAc), and 9.15 (s, 13-Me), which was dissolved in dry methanol (100 ml) and heated under reflux for 2 h. After dilution with water, the solution was extracted with ether (×2). The combined extracts were washed with sodium hydrogen carbonate solution and dried. Removal of the solvent gave a gum which was hydrolysed by heating under reflux in aqueous methanolic potassium hydroxide (2%; 100 ml) for 30 min. The usual work-up afforded a mixture which was dissolved in benzene (150 ml) containing ethylene glycol (15 ml) and toluene-*p*-sulphonic acid (200 mg). This solution was heated under

reflux for 18 h and the usual work-up afforded the *methoxy-ethylenedioxy-19-hydroxy-compound* (43) (3.5 g), m.p. 167—170° (from methanol), $[\alpha]_D$ −76.5° (*c* 1.1), $\nu_{max.}$ 3 480 cm^{-1} (OH), τ 4.2—4.4 (m, 6-H), 6.15 (s, $-O-CH_2-CH_2-O-$), 6.25 (q, 19-H_2), 6.70 (s, OMe), 6.7—7.2 (m, 3-H), and 9.1 (s, 13-Me) (Found: C, 72.9; H, 9.5. $C_{22}H_{34}O_4$ requires C, 72.9; H, 9.45%).

17,17-*Ethylenedioxy*-3β-*methoxyandrost*-5-*en*-19-*al* (4).—Chromium trioxide (3.2 g) was added to a stirred solution of pyridine (4.8 g) in dichloromethane (70 ml). Stirring was continued for 30 min, after which a solution of the methoxy-ethylenedioxy-19-hydroxy-compound (43) (2 g) in dichloromethane (30 ml) was added in one portion. After a further 30 min, the mixture was filtered and the residue well washed with ether. The combined filtrate and washings were then washed successively with aqueous 2N-sodium hydroxide, 2N-hydrochloric acid, sodium hydrogen carbonate solution, and brine, and dried. Removal of the solvent gave the *methoxy-aldehyde* (4) (1.4 g), m.p. 128—130° (from methanol), $[\alpha]_D$ −258° (*c* 0.4), $\nu_{max.}$ 1 720 cm^{-1} (C=O), τ 0.3 (s, 19-H), 4.05—4.25 (m, 6-H), 6.15 (s, $-O-CH_2-CH_2-O-$), 6.7 (s, OMe), 6.7—7.2 (m, 3-H), and 9.2 (s, 13-Me) (Found: C, 73.2; H, 9.0. $C_{22}H_{32}O_4$ requires C, 73.3; H, 8.95%).

17,17-*Ethylenedioxy*-3β-*methoxy*-19-*methyleneandrost*-5-*ene* (8).—A 2.3M-solution of n-butyl lithium in hexane (2 ml) was added, under nitrogen, to a suspension of methyltriphenylphosphonium iodide (2 g) in dry benzene. The clear solution was stirred for 2 h at room temperature, after which a solution of the aldehyde (4) (1 g) in dry benzene (50 ml) was added dropwise over 30 min. Stirring was continued overnight after which the mixture was heated under reflux for 4 h. The usual work-up and chromatography on silica gel [eluting with ethyl acetate–benzene (1 : 5)], gave the methoxy-ethylenedioxy-diene (8) (500 mg), m.p. 116—118° (from methanol), $[\alpha]_D$ +15.6° (*c* 0.6), τ 4.0—4.55 (m, RC*H*=CH_2 and 6-H), 4.55—5.3 (m, RCH=CH_2), 6.13 (s, $-O-CH_2-CH_2-O-$), 6.7—7.0 (m, 3-H), 6.68 (s, OMe), and 9.25 (s, 13-Me) (Found: M^+, 358.2514. Calc. for $C_{23}H_{34}O_3$: *M*, 358.2508).

5,6α-*Epoxy*-17,17-*ethylenedioxy*-3β-*methoxy*-19-*methylene*-5α-*androstane* (14).—An ethereal solution of the methoxy-ethylenedioxy-diene (8) (400 mg) was treated with an excess of monoperphthalic acid in ether in the usual manner to give, after preparative t.l.c. [eluting with ethyl acetate–benzene (1 : 5)], the methoxy-ethylenedioxy-epoxide (14) (150 mg), m.p. 102—103° (from dichloromethane–ether–petroleum), $[\alpha]_D$ −118° (*c* 1.6), τ 4.25 (m, RC*H*=CH_2), 4.5—5.2 (m, RCH=CH_2), 6.18 (s, $-O-CH_2-CH_2-O-$), 6.35—6.8 (m, 3-H), 6.73 (s, OMe), 7.0 (d, *J* 3.5 Hz, 6-H), and 9.3 (s, 13-Me) (Found: M^+, 374.2453. Calc. for $C_{23}H_{34}O_4$: *M*, 374.2457).

6β-*Acetoxy*-5-*hydroxy*-3β-*methoxy*-19-*methylene*-3α-*androstan*-17-*one* (31).—Treatment of a solution of the methoxy-ethylenedioxy-epoxide (14) (150 mg) in ethyl methyl ketone (20 ml) with aqueous perchloric acid (60%; 0.05 ml) in the usual way gave the crude dihydroxy-ketone (26), which was acetylated with acetic anhydride (0.3 ml) in pyridine (1 ml) at 100 °C for 2 h. The usual work-up and preparative t.l.c. [eluting (× 3) with ethyl acetate–benzene (1 : 1)] gave the methoxy-acetoxy-5α-hydroxy-ketone (31) (80 mg), a gum, $[\alpha]_D$ +51.6° (*c* 3.5), $\nu_{max.}$ 3 450 (OH), 1 740 and 1 720 (C=O), and 1 250 cm^{-1} (C–O), τ 3.55 (m, RC*H*=CH_2), 4.5—5.2 (m, RCH=CH_2 and 6-H), 6.1—6.6 (m, 3-H), 6.75 (s, OMe), 7.9 (s, OAc), and 9.22 (s, 13-Me) (Found: M^+, 390.2397. $C_{23}H_{34}O_5$ requires *M*, 390.2406).

3β,6β-*Diacetoxy*-5-*ethenyl*-19-*nor*-5β-*cholest*-9-*ene* (32).—A solution of the hydroxy-diacetate (28) (80 mg) in acetic acid (6 ml) and acetic anhydride (1 ml) was treated with a solution of sulphuric acid in acetic acid (1.6M; 0.1 ml) and set aside at room temperature for 6 h. The solution was poured into brine and the resultant mixture was extracted with ether. The combined extracts were washed with sodium hydrogen carbonate solution and water. Preparative t.l.c. of the product obtained by evaporation [eluting with ethyl acetate–benzene (1 : 10)] gave the diacetate (32) (44 mg), a gum, $[\alpha]_D$ +73° (*c* 1.0), $\nu_{max.}$ 1 740 (C=O) and 1 250 cm^{-1} (C–O), τ (CCl_4) 4.28 (m, RC*H*=CH_2), 4.65—5.5 (m, RCH=CH_2, 3- and 6-H), 8.05 (s, OAc), 8.1 (s, OAc), and 9.18 (s, 13-Me) [Found: *m/e*, 438.3496. Calc. for *M* ($C_{32}H_{50}O_4$) — AcOH: *m/e*, 438.3498].

3β,6β-*Diacetoxy*-5-*ethenyl*-19-*nor*-5β-*androst*-9-*en*-17-*one* (34).—A 0.25M-solution of sulphuric acid in acetic acid (4 ml) was added to a solution of the hydroxy-diacetate (30) (300 mg) in acetic anhydride in acetic acid (10%; 22 ml) at 30—35 °C. The solution was maintained at this temperature for 30 min, poured into brine, and worked-up as above. Preparative t.l.c. of the product [eluting (× 2) with ether–petroleum (2 : 1)] gave the diacetate (34) (80 mg), m.p. 146—147° (from methanol), $[\alpha]_D$ +167° (*c* 0.2), $\nu_{max.}$ 1 740 (C=O) and 1 250 cm^{-1} (C–O), τ 4.25 (m, RC*H*=CH_2), 4.6—5.4 (m, RCH=CH_2, 3- and 6-H), 7.95 (s, OAc), 8.0 (s, OAc), and 9.0 (s, 13-Me) [Found: *m/e*, 340.2042. Calc. for *M* ($C_{24}H_{32}O_5$) — AcOH: *m/e*, 340.2038].

6β-*Acetoxy*-5-*ethenyl*-3β-*methoxy*-19-*nor*-5β-*androst*-9-*en*-17-*one* (35).—A 0.25M-solution of sulphuric acid in acetic acid (0.6 ml) was added to a stirred solution of the methoxyacetoxy-5α-hydroxy-ketone (31) (70 mg), in acetic anhydride in acetic acid (10%; 3 ml) at 30—35 °C. After 15 min the mixture was worked up as above and gave the *methoxy-acetate* (35) (40 mg), m.p. 148—150° (from methanol), $[\alpha]_D$ +174° (*c* 0.5), $\nu_{max.}$ 1 735 cm^{-1} (C=O), τ 4.15 (m, RC*H*=CH_2) 4.4—5.5 (m, RCH=CH_2 and 6-H), 6.4—6.6 (m, 3-H), 6.73 (s, OMe), 7.95 (s, OAc), and 9.0 (s, 13-Me) (Found: C, 73.9; H, 8.8. $C_{23}H_{32}O$ requires C, 74.15; H, 8.65%).

5-*Ethyl*-19-*nor*-5β-*cholest*-9-*ene*-3β,6β-*diol* (44).—A solution of the diacetate (32) (30 mg) in methanolic potassium hydroxide (1%; 10 ml) was heated under reflux for 15 min. The usual work-up afforded the diol (36) (20 mg), τ (CCl_4) 4.05 (m, RC*H*=CH_2), 4.6—5.4 (m, RCH=CH_2), 6.1 (m, 3-H), 6.6 (m, 6-H), and 9.2 (13-Me). A solution of the diol (36) (15 mg) in ethyl acetate was stirred with palladium–charcoal (5%; 10 mg) in hydrogen for 1 h. Filtration and evaporation gave the *diol* (44) (14 mg), a gum, τ 6.0—6.3 (m, 3-H), 6.4—6.8 (m, 6-H), and 9.2 (13-Me) (Found: C, 81.25; H, 11.5. $C_{28}H_{48}O_2$ requires C, 80.7; H, 11.6%).

3β,6β-*Diacetoxy*-5-*ethenyl*-19-*nor*-5β,10α-*cholestane*-9α,10-*diol* (46).—A solution of the diacetate (32) (60 mg) in pyridine (3 ml) was treated with osmium tetraoxide (30 mg) and the mixture was kept at room temperature for 24 h. Chloroform was added and the solution was saturated with hydrogen sulphide. Filtration through a short column of alumina and evaporation gave a crude product which, after preparative t.l.c. [elution with benzene–ethyl acetate (3 : 1)], gave the diol (46) (35 mg), a gum, $\nu_{max.}$ 1 740 (C=O) and 3 500 cm^{-1} (OH), τ (CCl_4) 3.7—5.3 (m, RCH=CH_2, 3- and 6-H), 7.96 (s, OAc), 8.15 (s, OAc), and (s, 13-Me).

3β,6β-*Diacetoxy*-5-*ethenyl*-19-*nor*-9,10-*seco*-5β-*cholestane*-9,10-dione (48).—A solution of the diol (46) (30 mg) in t-butyl alcohol (3 ml) was treated with a 0.065M-solution of lead tetra-acetate in acetic acid (4 ml) and maintained at 45 °C for 4 h. The mixture was poured into water and

extracted with ether, and the extract was washed with sodium hydroxide solution (1%) and water, and dried. Removal of the solvent gave the diketone (48) (20 mg), a gum, $\nu_{max.}$ 1 740 and 1 720 cm^{-1} (C=O), τ 3.8—6.2 (m, RCH=CH_2,3- and 6-H), 8.05 (s, OAc), 8.12 (s, OAc), and 9.05 (s, 13-Me) (Found: M^+, 530.3597. Calc. for $C_{32}H_{50}O_6$: M, 530.3607).

3β,6β-*Diacetoxy*-9α,10-*epoxy*-5-*ethenyl*-19-*nor*-5β,10α-*cholestane* (47).—A solution of the diacetate (32) (100 mg) in ether (2 ml) was treated with an excess of monoperphthalic acid in ether in the usual manner and gave the *epoxide* (47) (80 mg), m.p. 98—100° (from methanol), $[\alpha]_D$ +22° (*c* 0.7), τ (CCl_4) 4.0—5.3 (m, RCH=CH_2, 3- and 6-H), 8.10 (s, OAc), 8.11 (s, OAc), and 9.25 (s, 13-Me) (Found: C, 74.55; H, 9.8. $C_{32}H_{50}O_5$ requires C, 75.65; H, 9.8%).

17,17-*Ethylenedioxy*-19-*hydroxy*-3β-*methoxy*[19-^{2}H]*androst*-5-*ene* (50).—A solution of the aldehyde (4) (400 mg) in ether (50 ml) was added slowly to a stirred suspension of lithium aluminium deuteride (50 mg) in ether (10 ml) at −10 °C. The suspension was allowed to warm to room temperature and heated under reflux for 30 min. Ethyl acetate was cautiously added to the cooled mixture, which was then filtered. The residue was washed with ether and the combined washings and filtrate were dried and evaporated to afford the deuterio-alcohol (50) (360 mg), τ 4.1—4.4 (m, 6-H), 6.1br (s, 19-H and $-O-CH_2-CH_2-O-$), 6.65 (s, OMe), 6.7—7.2 (m, 3-H), and 9.08 (s, 13-Me).

19ξ-*Hydroxy*-3β-*methoxy*[19-^{2}H]*cholest*-5-*ene* (51).—A solution of the methoxy-aldehyde (2) [11] (2.5 g) in ether (200 ml) was added to a stirred suspension of lithium aluminium deuteride (250 mg) in ether (100 ml) at −10 °C. The mixture was treated as above and gave the crude deuterio-alcohol (51) (2.3 g), the bulk of which was used without purification. A sample crystallised from methanol had m.p. 160—162°, $[\alpha]_D$ −26° (*c* 1.0), τ 4.2—4.4 (m, 6-H), 6.1—6.3 (m, 19-H), 6.66 (s, OMe), 6.8—7.2 (m, 3-H), and 9.3 (s, 13-Me).

3β-*Methoxy*-19-*methylene*-5α-*cholestane*-5,6β-*diol* (24) (*Essentially* 19-*Deuteriated*).—A solution of the deuteriated epoxide (2) [11] (750 mg), prepared from the deuterio-alcohol (51) by the procedures already outlined, was treated in the usual manner with aqueous perchloric acid in ethyl methyl ketone and gave the essentially 19-deuteriated diol (24) (400 mg), m.p. 204—205° (from aqueous methanol), $[\alpha]_D$ +41.5° (*c* 2.2), τ 4.7 and 5.2 (narrow m, RCD=CH_2), 6.2—6.6 (m, 3- and 6-H), 6.7 (s, OMe), and 9.41 (s, 13-Me) [Found: C, 77.8; H, 11.6. Calc. for $C_{29}H_{49}DO_3$: C, 77.8; H(D), 11.5%).

6β-*Acetoxy*-3β-*methoxy*-19-*methylene*-5α-*cholestan*-5α-*ol* (29) (*Essentially* 19-*Deuteriated*).— The deuteriated diol (24) (350 mg) was acetylated to give, after preparative t.l.c., the essentially 19-deuteriated methoxy-acetate (29) (250 mg), a gum, $[\alpha]_D$ +13.5° (*c* 2.6), τ 4.65 and 4.96 (narrow m, RCD=CH_2), 5.1 (m, 6-H), 6.2—6.6 (m, 3-H), 6.62 (s, OMe), 7.92 (s, OAc), and 9.41 (s, 18-Me).

6β-*Acetoxy*-5-*ethenyl*-3β-*methoxy*-19-*nor*-5β-*cholest*-9-*ene* (33) (*Essentially* α-*Deuteriated in the Ethenyl Group*).—The deuteriated methoxy-acetate (29) (150 mg) rearranged under the usual conditions to give, after preparative t.l.c. [eluting (× 3) with ethyl acetate–benzene (1 : 2)] the deuteriated Δ^9-compound (33) (60 mg), a gum, $[\alpha]_D$ +112° (*c* 1.26), τ 4.70—5.4 (m, RCD=CH_2 and 6-H), 6.4—6.7 (m, 3-H), 6.72 (s, OMe), 7.97 (s, OAc), and 9.2 (s, 13-Me).

We thank the S.R.C. for research studentships (to J. G. Ll. J. and I. G. G.), and Beecham Research Laboratories for a research grant (to B. W. C.). High resolution mass spectra were determined by the P.C.M.U., Aldermaston, and financed by the S.R.C.

[7/265 *Received*, 14*th February*, 1977]