SOME ASPECTS OF STEROIDAL

EPOXIDE REARRANGEMENTS

A Thesis

submitted by

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in Partial Fulfilment of the Requirements for

the Degree of Doctor of Philosophy

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September, 1971.

Summary:-

The reactions of 5,6α-epoxy-3β-hydroxy-5α-cholestane, 5,6β-epoxy-3β-hydroxy-5β-cholestane, and 5,6α-epoxy-3β-methoxy-5α-cholestane with boron trifluoride etherate in benzene give largely products of rearrangement via C(5)-O cleavage. These results contrast with the known reactions of the corresponding 3β-acetoxy-epoxides which give high yields of fluorohydrins.

The 3β-acetoxy-,3β-hydroxy-,and 3β-methoxy-, derivatives of 5,6α-epoxy-5α-androstan-17-one and 5,6α-epoxy-5α-pregnan-20-one react with boron trifluoride etherate in benzene to give, in addition to their respective fluorohydrins, products of rearrangement via C(5)-O cleavage. 5,6β-Epoxy-3β-hydroxy-5β-androstan--17-one and 5,6β-epoxy-3β-hydroxy-5β-pregnan-20-one were found to react with boron trifluoride in a similar manner.

In contrast to their cholestane analogues 3β-acetoxy-, 3β-hydroxy-, and 3β-methoxy-, substituted 5,6α-epoxy-19-methyl-5α-cholestanes react with boron trifluoride etherate in benzene to give reduced yields of their respective backbone-rearranged compounds and a greater diversity of products derived from C(5)-O cleavage, including a number of 1(10→5)-abeo-steroids. 3β-Acetoxy-5,6β-epoxy-19--methyl-5β-cholestane gives the backbone-rearranged compound and 3β-acetoxy-5-formyl-19-methyl-B-nor-5β--cholestane as major products when treated with boron trifluoride.

The 3α-acetoxy-, and 3α-hydroxy-, substituted 5,6α-epoxy-
-19-methyl-5α-cholestanes when treated with boron trifluoride
in benzene give a diverse array of products derived from
C(5)-O cleavage and none of their respective fluorohydrins.
3α-Acetoxy-5,6β-epoxy-19-methyl-5β-cholestane reacts with
boron trifluoride to give 3α-acetoxy-19-methyl-5α-cholestan-
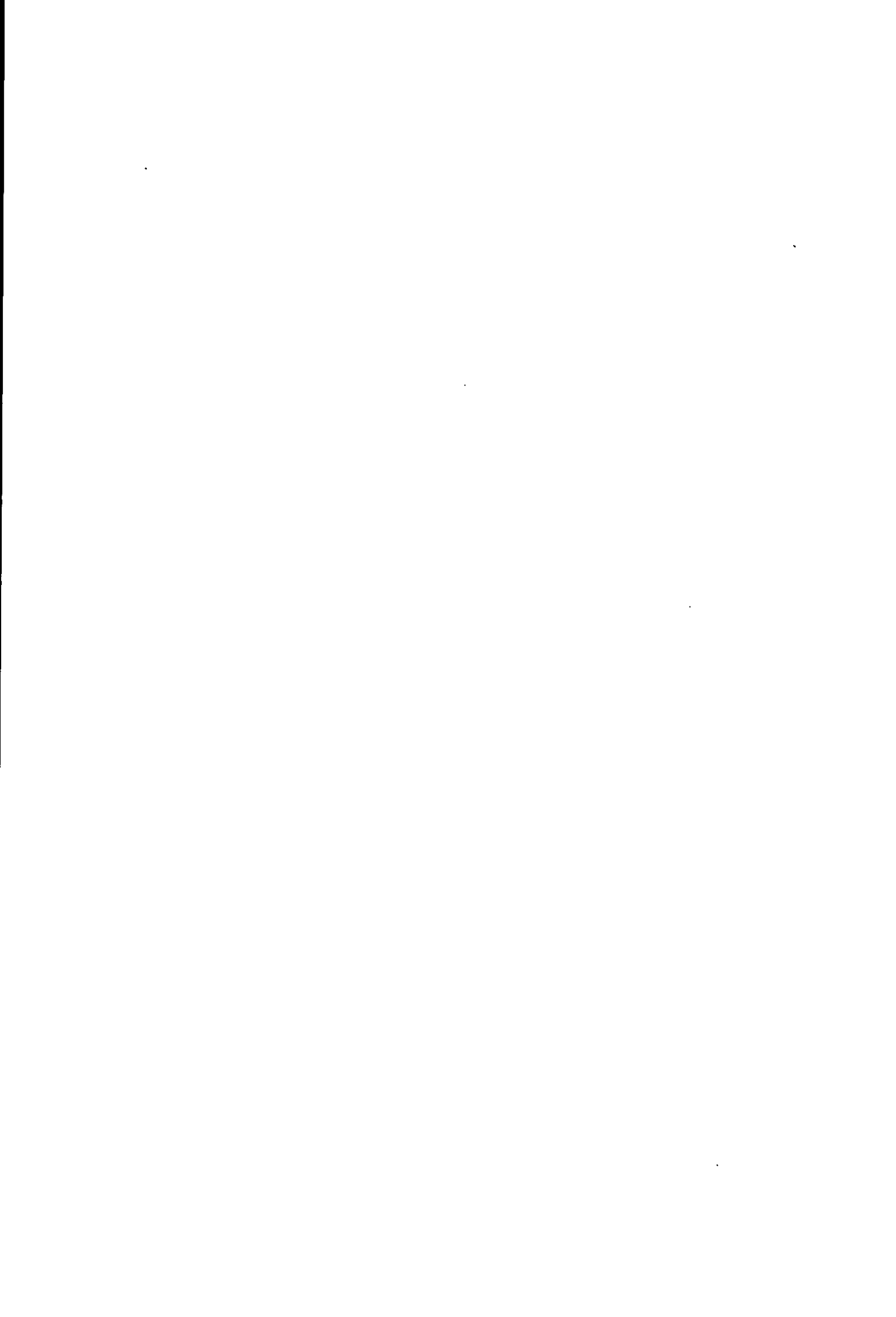-6-one and 5-acetoxy-3α,6β-dihydroxy-19-methyl-5α-cholestane.

3β-Acetoxy-,3β-hydroxy-, and 3β-methoxy-, substituted
5,6α-epoxy-19-methylene-5α-cholestanes react with boron
trifluoride to give their respective fluorohydrins in
addition to rearrangement products derived from initial
C(5)-O cleavage.

The above reactions are discussed qualitatively, in
terms of the steric and electronic effects of the C(3)-,
C(17)- and C(19)-substituents, and their effects on the
competition between C(5)-O cleavage and fluorohydrin formation.
The nature and diversity of the products obtained have been
rationalised in terms of a carbonium ion type of mechanism.

The 6-keto-,6β-acetoxy-,and 6-desoxy-,derivatives
of 9,10-epoxy-3β-methoxy-5-methyl-19-nor-5β,10α-cholestane
and 9,10-epoxy-3β-methoxy-5-methyl-19-nor-5β,9β-cholestane
react with boron trifluoride in benzene to give rearrangement
products including backbone-rearranged products in addition
to their respective $\triangle^{9(10),11(12)}$- and $\triangle^{1(10),9(11)}$-compounds.
The direction of epoxide cleavage and the balance between
conjugated olefin formation and rearrangement is qualitatively
equated to the variation in inductive (-I) effects of the

C(6)-substituents. The greater yields of conjugated olefins
from the β-epoxides than the α-epoxides is ascribed to
the greater degree of C(9) carbonium ion character necessary for
migration of the 8β-hydrogen atom in the former compounds.
3β-Acetoxy-8,9-epoxy-5α,8α-lanostane reacts with boron
trifluoride etherate in benzene to give 3β-acetoxy-5α-lanosta –
-7,9(11)-diene. Under similar conditions 3β-acetoxy-9,11α-
-epoxy-5α-lanostane gives a mixture of 3β-acetoxy-5α,9β-
-lanostan-11-one and 3β-acetoxy-8-methyl-18-nor-5α,8α,14β-lanosta-
9(11),13(17)-diene. Treatment of 3β-acetoxy-5α-lanost-9(11)-ene
with N-bromoacetamide and perchloric acid gives 3β-acetoxy-
-7α-bromo-5α-lanost-8-en-11-one.

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INTRODUCTION:-

The epoxide ring may be opened using either an acid or
Lewis acid catalyst in a non-polar solvent and in the absence
of any effective nucleophiles, rearrangements may be induced.
Any trisubstituted epoxide has an electronic preference for
cleavage of the tertiary carbon oxygen bond.

In the first systematic investigation of the reaction
of some steroidal epoxides with boron trifluoride diethyletherate
Henbest[1a] found that a wide variety of steroidal epoxides
gave ketones as their major products, the remaining materials
being unidentifiable.

The ketones are formed by a stereospecific hydride shift
to the electron deficient carbon atom, produced by polarisation
or fission of a carbon oxygen bond in the epoxide Lewis acid
complex which is first formed.

Subsequent work[1b] on the reaction of some 3β-
-substituted 5,6-epoxy cholestanes (Ia,b) showed the
formation of fluorohydrins (IIa,b) instead of the ketones
(IIIa,b). Again some non-identifiable residues were obtained.
The formation of the fluorohydrins was attributed to the
presence of fluoride ions in the boron trifluoride. The
slow formation of the fluorohydrins can only compete with
the rapid formation of the ketones when the polarisation of
the C(5)-O bond is sufficiently inhibited by an electronegative
substituent at C(3). It was also suggested that the move-
ment of a 3β-substituent from an equatorial to a less

1.

I

R
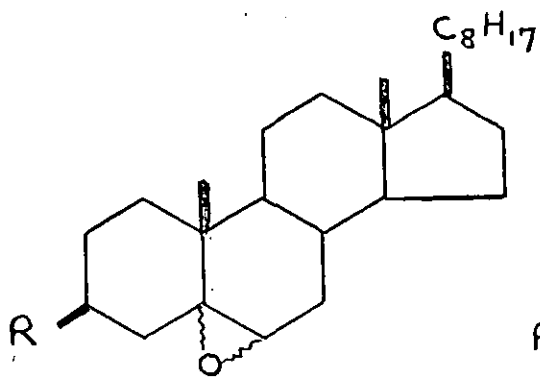
(a) 5,6α   OAc
(b) 5,6α   Cl
(c) 5,6α   H
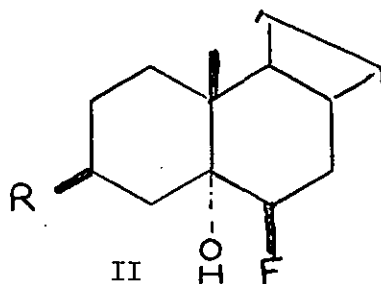
II

R

(a)   OAc
(b)   Cl

III

R

(a)   OAc
(b)   Cl
(c)   H
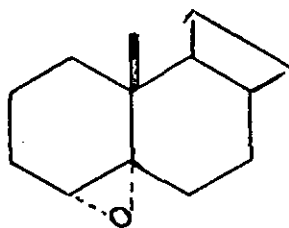
IV
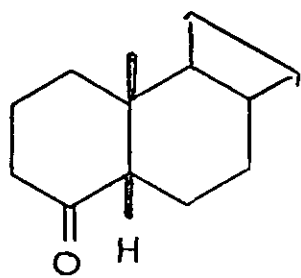
V
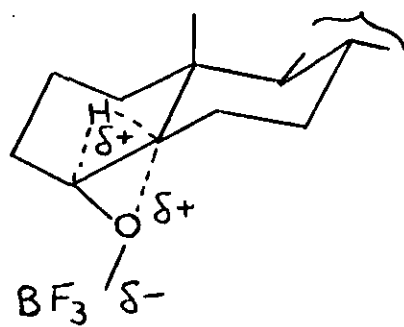
VI

favourable axial conformation in the formation of products

having 5β-stereochemistry would inhibit the formation of

these products. Subsequent work has shown that the yields

of fluorohydrins may be substantially reduced by the use

of freshly purified boron trifluoride diethyletherate.[2]

The initial suggestion[1b] that the formation of a

ketone from an epoxide was unfavourable if it led to

formation of a cis-decalin type of structure or one strained

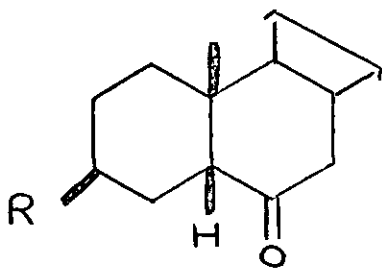by large syn-diaxial interactions implies that the transition

state determining the overall reaction path has a resemblance

to the final product.[3] Thus, in the rapid and efficient

conversion of the epoxy-cholestane (IV) to the ketone (V)

a transition state (VI) derived from compound (IV) involves

distortion only of ring A, towards its final conformation in

the product (V). However, in the slow and inefficient

conversion of the epoxide (Ic) to the ketone (IIIc) the

comparable transition state (VII) has no conformational

resemblance to the product. The transition state (VIII)

which would resemble the product in this case would involve

the energetically unfavourable distortion of the A and B

rings simultaneously.

Failure to give a ketone has therefore been interpreted[3]

as conformational or steric frustration of the formation of

the necessary transition state. Electrostatic or inductive

effects of any neighbouring groups have also to be taken into

consideration. In the cases where these effects are operative
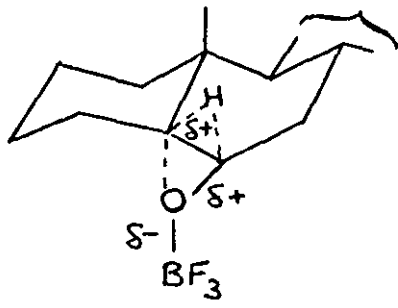
VII
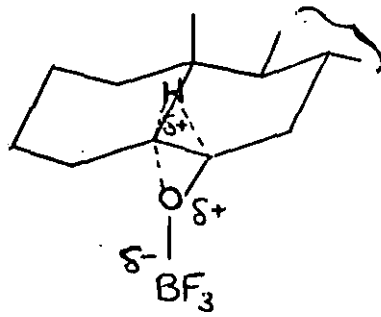
VIII
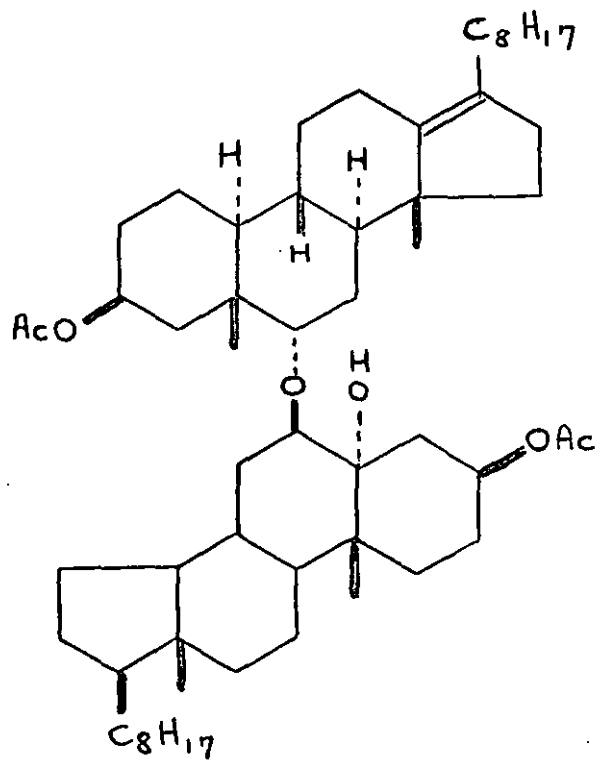
IX

an alternative pathway of elimination or rearrangement followed by elimination is pursued.[3]

In a re-examination of the reaction of 3β-acetoxy-5,6α-epoxy-cholestane (Ia) with boron trifluoride, first investigated by Henbest,[1b] Hartshorn et.al.[2] found that, depending upon the reaction conditions, a yield of up to 32% of a hydroxylic olefin was obtained in addition to the fluorohydrin (IIa). The olefin was assigned the dimeric structure (IX). The 13,17-olefinic bond is formed by C(5)-O cleavage of the epoxide (Ia), accompanied by a series of stereospecific trans-1,2-shifts of the groups at all the tertiary centres of the steroid nucleus to give the 'backbone-rearranged' compound (IX) having an inverted stereochemistry at each tertiary centre. Many examples of such rearrangements of epoxides to give backbone-rearranged compounds (usually as monomers) are well documented.[3] Similar rearrangements in the acid catalysed isomerisation of steroid and terpenoid olefins have also been observed and recently reviewed.[4a,b]

These 'backbone rearrangements' although superficially set up for a concerted process are unlikely to be completely so. Such concerted mechanisms would involve a simultaneous flattening of the four rings of the steroid and this would be energetically unfavourable, the calculated energy difference between the chair and half chair cyclohexane ring being 15 k.cal.mole.$^{-1}$ [5]

X

(a) 5,6α
(b) 5,6β
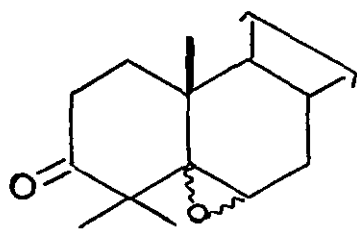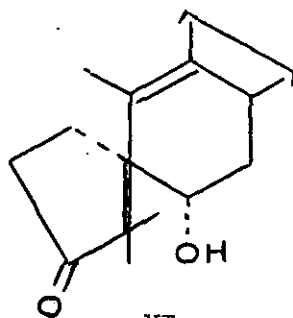
XI
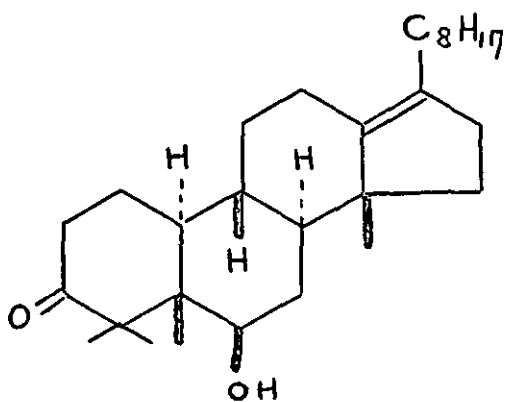
XII
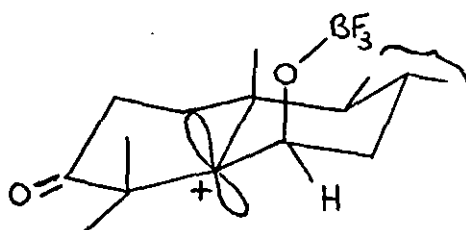
XIII

The intermediacy of discrete carbonium ions is indicated in the reactions of the two 4,4-dimethyl-5,6-epoxy-cholestan--3-ones (Xa,b) with boron trifluoride.[6,7] Compound (Xa) gave as the only product the spiro-compound (XI), and compound (Xb) gave the backbone-rearranged compound (XII) (80%). The formation of a 6-ketone from the conformation (XIII) of the intermediate carbonium ion from compound (Xb) would be unfavourable since the 6α-hydrogen is held in the nodal plane of the carbonium ion.[6] Although the effect of the differences in solvents and reagents cannot be accurately assessed it is of interest to note that the analogous backbone-rearrangements of some steroid and terpenoid olefins have recently been interpreted both in terms of concerted mechanisms [8,9] and equilibrating carbonium ion mechanisms.[4b, 10] Recently evidence has also been presented for a carbonium ion mechanism in the Westphalen rearrangement of 5α-hydroxy--steroids.[11,12]

To provide further information on the precise roles of electronic, conformational and steric factors in controlling the rearrangements of trisubstituted steroidal epoxides a study has been made of the boron trifluoride-catalysed reactions of some 5,6-epoxides, with varying substituents at C(3),C(17), and C(19). Information of this type should help to clarify the nature of the mechanism or competing mechanisms involved in these rearrangements.

C_8H_{17}

XIV

		R
(a)	5,6α	βOH,H
(b)	5,6β	βOH,H
(c)	5,6α	βOMe,H
(d)	5,6α	βOAc,H
(e)	5,6β	βOAc,H
(f)	5,6α	αOAc,H
(g)	5,6α	αOH,H
(h)	5,6β	αOAc,H
(i)	5,6α	βF,H

XV

	R
(a)	βOH,H
(b)	βOAc,H
(c)	αOH,H
(d)	βF,H

XVI

		R
(a)	5α	H
(b)	5β	H
(c)	5β	Me
(d)	5β	Ac
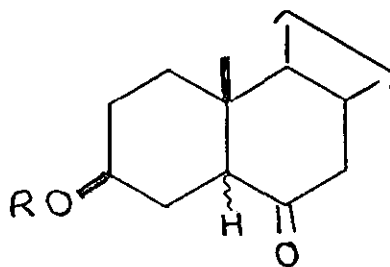
XVII

	R	R'
(a)	βOH,H	αOH,H
(b)	βOAc,H	αOAc,H
(c)	=O	=O
(d)	βOMe,H	αOAc,H
(e)	βOMe,H	=O
(f)	βOMe,H	αOH,H

Discussion 1 :-

Treatment of 5,6α-epoxy-3β-hydroxy-5α-cholestane (XIVa)

with boron trifluoride gave a mixture. Separation by

preparative t.l.c. gave the fluorohydrin (XVa)[14] (2%),

the C(6)-ketones (XVIa)[15] (4.5%) and (XVIb)[16] (11%),

the Westphalen derivative (XVIIa) (7%) and the backbone-

rearranged product (XVIIIa)[2] (10%) and a polar fraction.

The $[\alpha]_D$ value of the fluorohydrin (XVa) (-7.5°) was

considerably different from that previously reported,[14]

(+ 36°). However, the fluorohydrin was characterised as its

C(3)-acetate (XVb),[14] the spectroscopic data for both

compounds being satisfactory. In addition, the change in

$[M]_D$ in preparing the C(3)-acetate (XVb) (-89°) compares

well with that observed (-96°) for the preparation of the

C(3)-acetate of 3β,5,6β-trihydroxy-5α-cholestane.[17]

The Westphalen derivative (XVIIa) was identified

by the ^{1}H n.m.r. chemical shifts of the 5β-methyl (τ8.62)

and the 13β-methyl (τ 9.23) groups, these being typical

of compounds of this type.[12] The 6β-proton also appears

as the expected quartet[18] (τ 6.59, J(apparent), ca.

11 Hz., 4 Hz.). Intense end absorption in the u.v. spectrum[19]

of the diacetate (XVIIb) ($\varepsilon_{215\ nm}$, 5000) and Jones

oxidation[20] of the diol (XVIIa) to the known diketone[21]

(XVIIc) confirmed the assigned structure.

Partial acetylation of the polar fraction using acetic

anhydride/pyridine followed by preparative t.l.c. gave

the mono-acetate (XVIIIb), the 3β-hydroxyl being axial

and relatively difficult to acetylate. Further acetylation

XVIII

	R	R'
(a)	βOH,H	αOH,H
(b)	βOH,H	βOAc,H
(c)	βOAc,H	βOAc,H
(d)	βOH,H	βOH,H
(e)	=O	=O
(f)	βOMe,H	αOAc,H
(g)	αOAc,H	αOH,H

XIX

XX

XXI

XXII

XXIII
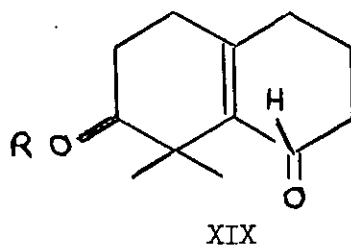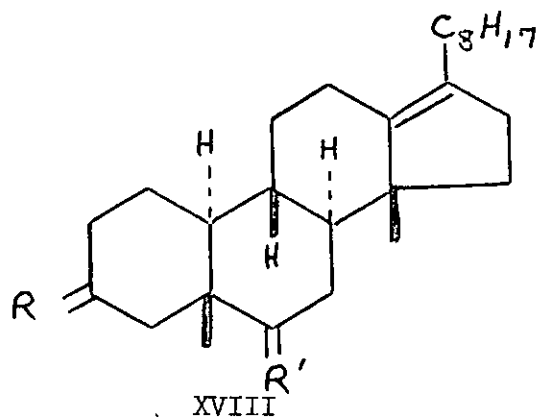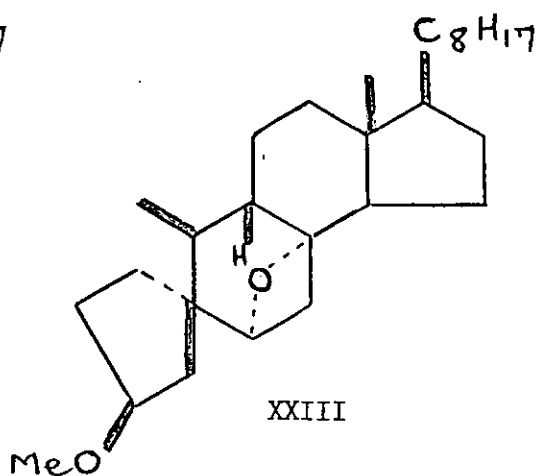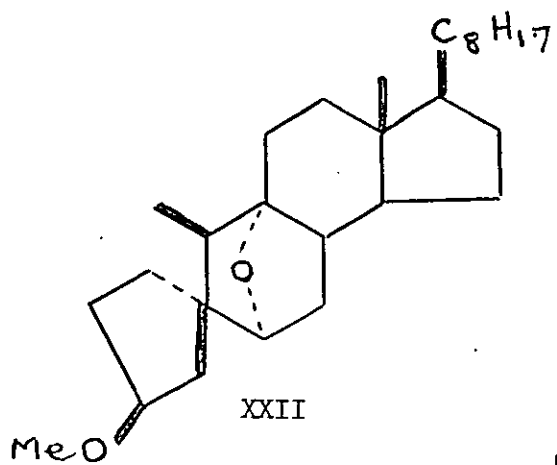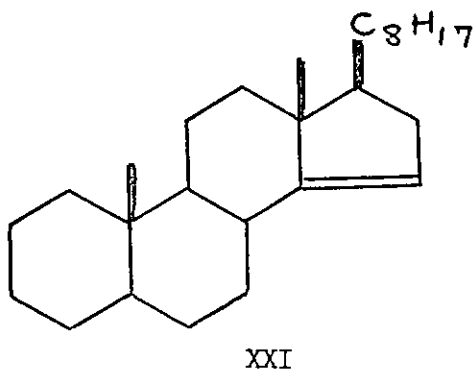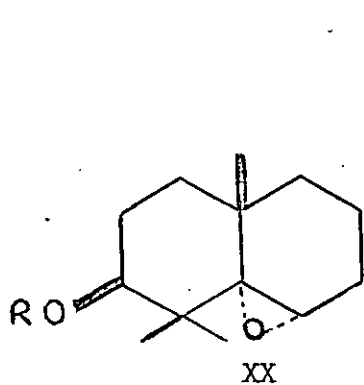
gave the known diacetate (XVIIIc) [2,22] (17%). Hydrolysis

of the diacetate (XVIIIc) to the diol (XVIIId) [2] and

oxidation gave the diketone (XVIIIe) [2] also obtained from

the diol (XVIIIa). The 6α-proton signal in the ^{1}H n.m.r.

spectrum of the diacetate (XVIIIc) appears as a triplet

(τ 5.42, J (apparent) ca. 7.8 Hz.), presumably owing to

the similarity of the chemical shifts of the 7α-and 7β-

protons. [23] The epimerisation at C(6) is thought to occur

through a C(10) or C(8) carbonium ion, as shown (fig.1).

A C(10) carbonium ion could exist in the conformations (1)

or (2), the former being the more preferable. [24] In

neither case is the C(5)-C(6) bond well disposed for cleavage,

being in the nodal plane of the vacant C(10) p-orbital. [25]

With a C(8) carbonium ion (3) the C(6)-C(7) bond is well

aligned (ca.30° to the p-orbital plane) for cleavage. [25]

In addition, in the case of the C(8) but not the C(10) carbonium

ion the recyclisation reaction could occur via a·six membered

transition state, with the intramolecular removal of the

C(9) hydrogen atom by the C(6) oxygen atom.

This scheme is similar to that recently proposed for

the epimerisation at C(4) in the rearrangement of a

4,5β-epoxide. [24] Recently Whitlock [26] has isolated

aldehydes of the general type (XIX) from the Lewis acid

and acid catalysed opening of some decalyl epoxides (XX).

However the extra conformational mobility of a decalyl

carbonium ion (fig.1 (4)) coupled with the presence of the
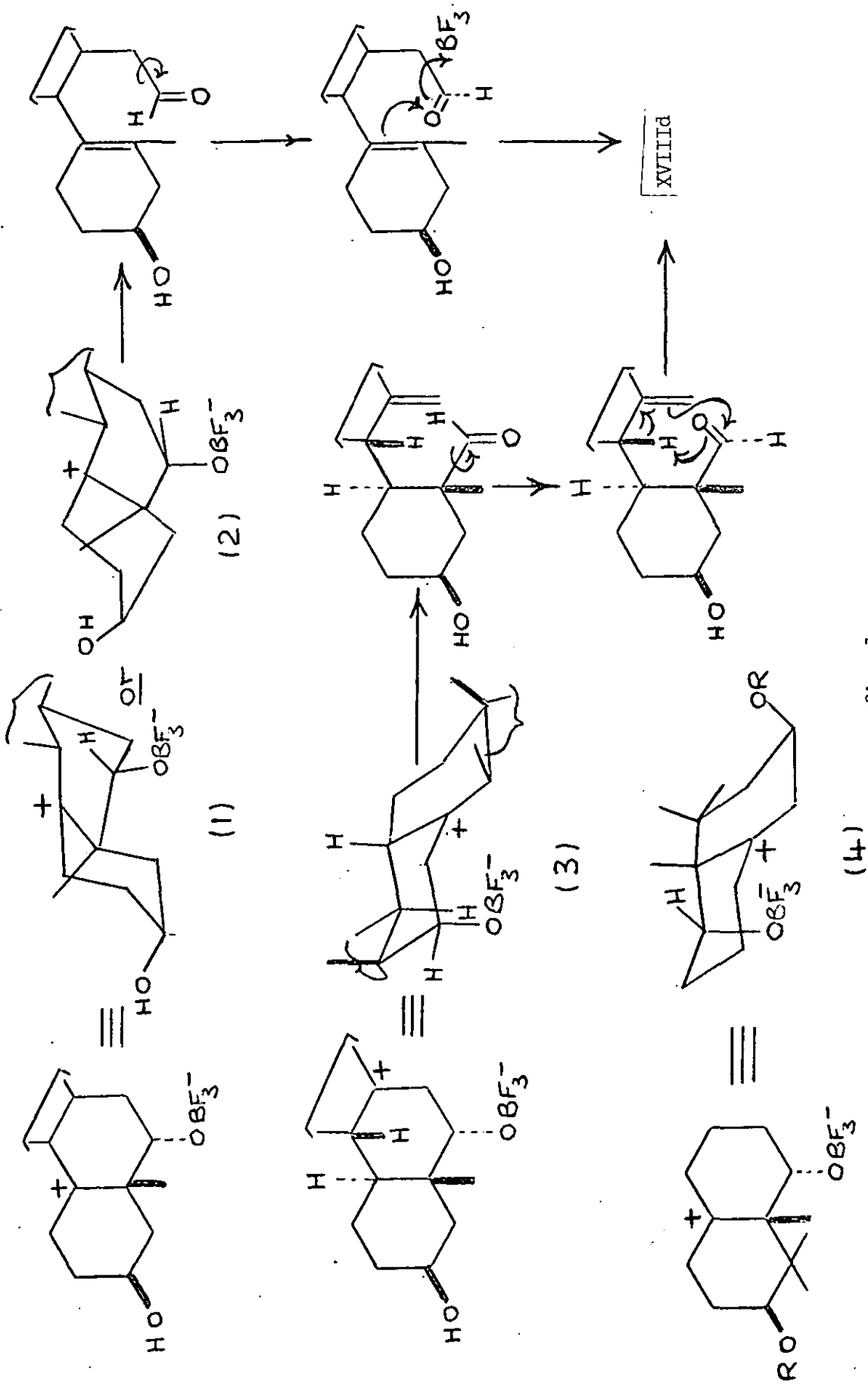
fig. 1

geminal dimethyl group may enable a conformation as illustrated (fig.1 (4)) to be attained in which fission of the C(5)-C(6) bond (steroid nomenclature) may occur.

Reactions formally similar to the proposed aldehyde recyclisation, involving the intramolecular attack of an olefin on an epoxide when treated with acid or Lewis acid, are well known.[27a,b,c]

Treatment of the diol (XVIIIa) with boron trifluoride gave recovered starting material. Similar treatment of the diol (XVIIa) gave only compound (XVIIIa) (as shown by t.l.c.). This indicated that neither compound (XVIIIa) or compound (XVIIa) were precursors of compound (XVIIId).

The ketone (XVIb) was shown to isomerise slowly on silica gel to give its isomer (XVIa), thus accounting for the isolation of some of the latter. It was shown (t.l.c.) that the isomerisation of compound (XVIb) to compound (XVIa) did not occur under the conditions of the reaction or work up procedure.

The mixture obtained by reaction of 5,6β-epoxy-3β--hydroxy-5β-cholestane[13] (XIVb) was separated by preparative t.l.c. to give two major fractions, one of which was the ketone (XVIa) (20%).

The second, more polar fraction was acetylated to give the diacetate (XVIIIc) (40%), purified by preparative t.l.c..

Preparative t.l.c. of the reaction mixture obtained from 5,6α-epoxy-3β-methoxy-5α-cholestane[28] (XIVc) gave four fractions, which were acetylated and further purified

by preparative t.l.c. to give the ketone (XVIc) (27%),

the Westphalen derivative (XVIId) (18%), the backbone-

rearranged product (XVIIIf) (9%) and a fourth non-acylable

material (7%). The Westphalen derivative (XVIId) was

readily identifiable from its ^{1}H n.m.r. spectrum, the

5β-methyl (𝜏 8.80) and 13β-methyl (𝜏 9.22) groups being

typical of a Δ ^{9,10}-compound.[12]   In addition the acetate

(XVIId) was hydrolysed and oxidised to give the known ketone

(XVIIe).[28]   The backbone-rearranged compound (XVIIIf)

was identified from its ^{1}H n.m.r. and mass spectra. The

former shows the 5β-methyl (𝜏 8.92) and 14β-methyl

(𝜏 9.12), the lower branch of the C(21) H$_3$ doublet appearing

at 𝜏 8.98. Double irradiation 88 Hz. downfield from the

latter caused its collapse to a singlet (𝜏 9.03), showing

the C(20) proton to be allylic and hence confirming the

presence of a 13,17 olefinic bond.[2]   The base peak in

the mass spectrum (see table) of compound (XVIIIf) (m/e

285) corresponds to the loss of acetic acid and the side

chain from the parent ion (m/e 458). This was confirmed

by accurate mass measurement. This important loss of side

chain is typical of backbone-rearranged compounds.[22]

Djerassi[29] has recently shown that the loss of side chain

in the mass spectral fragmentation of steroidal nuclear

olefins increases in importance as the olefinic bond approaches

the D-ring, such that, in the Δ^{14} compound (XXI) m/e

[M-113] becomes the base peak. The proposed allylic
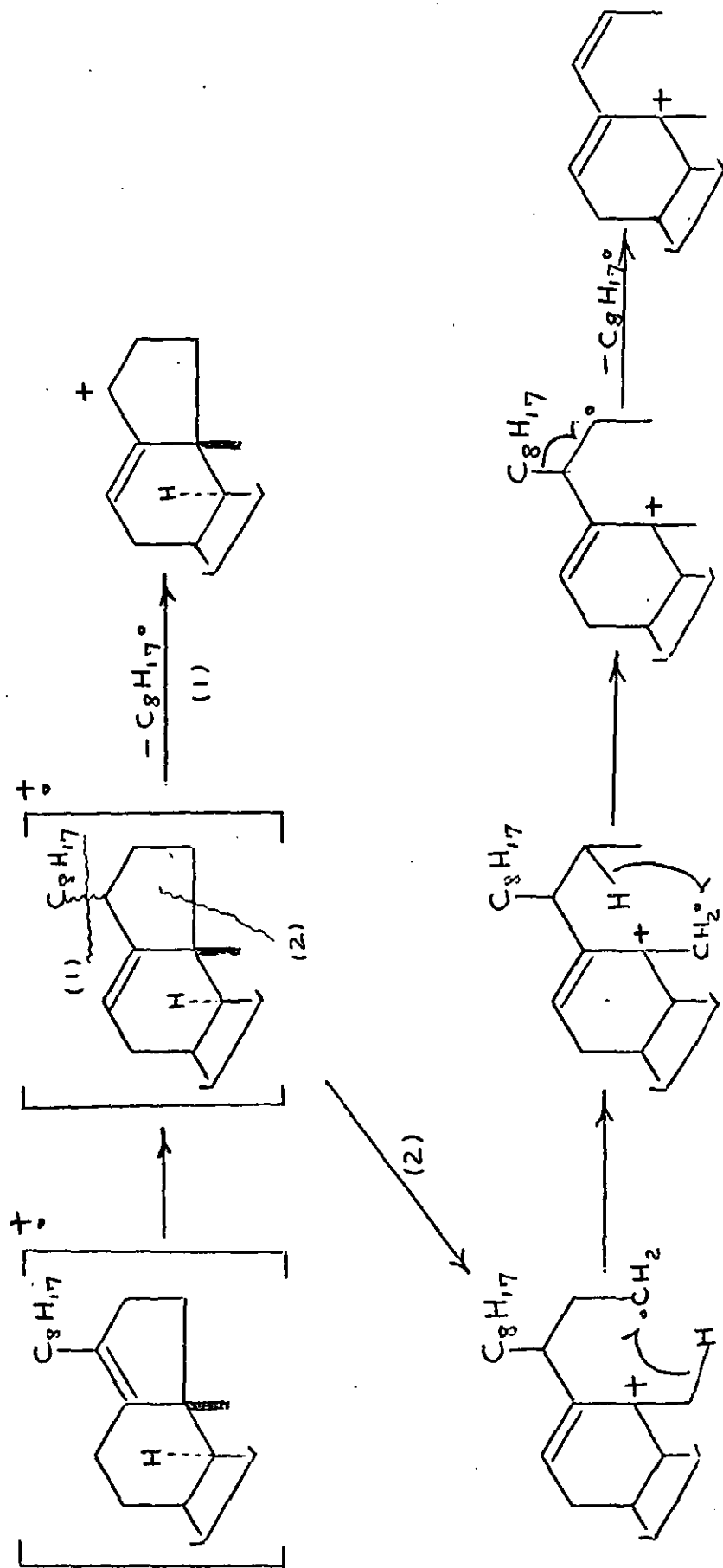
fig. 2

cleavage reactions responsible for the side chain loss in

$\Delta^{\underline{5}}$, $\Delta^{\underline{7}}$, and $\Delta^{\underline{14}}$, compounds cannot be directly

operable in the case of the $\Delta^{\underline{13,17}}$ compound. Direct

vinylic cleavage is also unlikely. The probable mechanism

is therefore one of olefin isomerisation in the molecular

ion,[30] prior to the allylic cleavage (fig.2), (1) or

(2). Fragmentation (2) is analogous to that proposed by

Djerassi for the $\Delta^{\underline{14}}$ compound (XXI).

The structure of the fourth compound (XXII) is based

on the following evidence. Analytical and mass spectral

(see table) data confirmed the molecular structure as

$C_{28}H_{48}O_2$. The i.r. spectrum shows no hydroxyl or carbonyl

bands indicating that the C(6) oxygen atom is involved in an

oxide linkage. The 220 M.Hz. ^{1}H n.m.r. spectrum of

compound (XXII) shows the C(6) proton signal as a doublet

(τ 6.17, J.ca. 5.2 Hz.) and the 10β-methyl signal as

a doublet (τ 9.09, J.7.5 Hz.). Consideration of these

data led to the two possible structures (XXII) and (XXIII).

An examination of molecular models revealed that the

observed doublet (J. ca. 5.2 Hz.) of the C(6) methine could

arise from either compound (XXII) or (XXIII), the dihedral

angle between one of the C(7) protons and the C(6) proton

being ca. 90° in each case. Similarly the chemical shift

of the C(6) proton could fit either structure.[31,32]

The preference for the structure (XXII) is based upon

further data obtained from related compounds (Discussions

2 and 3). The stereochemistry at C(5) is tentatively

XXIV

XXV

XXVI

XXVII
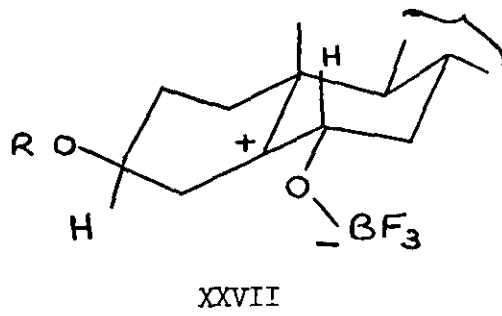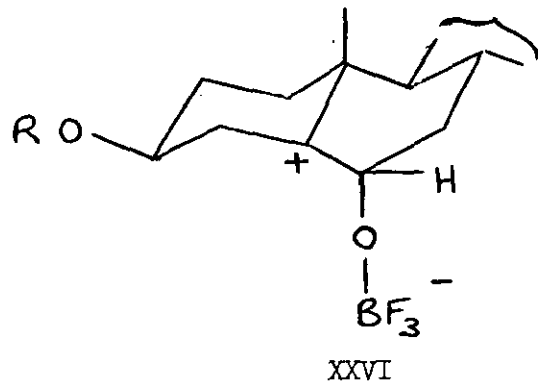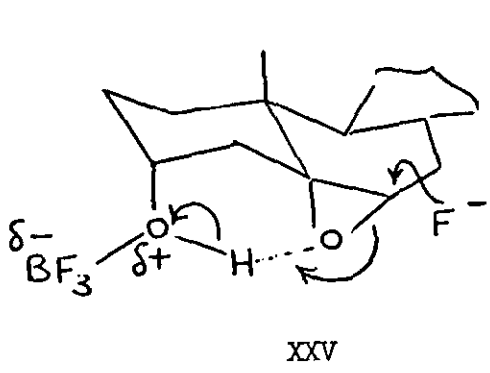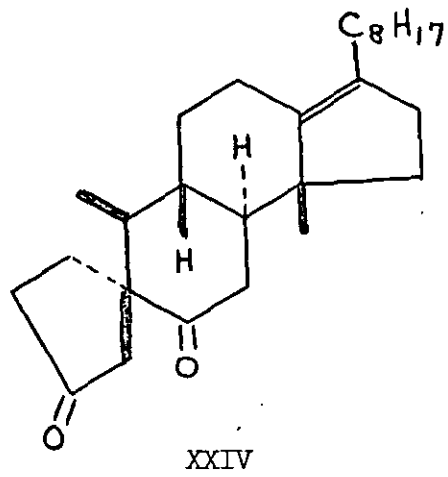
assigned from mechanistic considerations.

Treatment of the 6,9-oxide (XXII) with boron trifluoride/ acetic anhydride[33] gave a crude mixture which was hydrolysed and oxidised. Preparative t.l.c. gave the backbone-rearranged dioxo-spiran (XXIV). The i.r. spectrum of compound (XXIV) shows bands at 1750 cm.$^{-1}$ and 1715 cm.$^{-1}$ for the two carbonyl groups. The ^{1}H n.m.r. shows the 14β-methyl group (τ 9.08) superimposed on the high field branch of the C(21)H$_3$-doublet (τ 9.04, J ca. 5 Hz.). Double irradiation 83 Hz. downfield from this doublet caused its collapse to a shoulder on the 14β-methyl signal.[2] The base peak in the mass spectrum (see table)of compound (XXIV) (m/e 285) corresponds to the loss of side chain from the parent ion, confirming the $\triangle^{13,17}$ structure.[22]

Compound (XXII) is probably formed by intramolecular attack of the 6α-oxygen atom on a C(9) carbonium ion. The formation of both a 1,3 oxide bridge[31] and 1,4 oxide bridges[32,34] have been reported under similar conditions.

The possibility of proton release from the boron trifluoride co-ordinated 3β-hydroxyl group could be in part responsible for the low yield of fluorohydrin (XVa) from compound (XIVa). Such a dissociation could reduce the bulkiness of the 3β-substituent and conformationally facilitate C(5)-O-cleavage, or alternatively, the released proton could catalyse the epoxide opening. Both of these alternatives

may be discounted in view of the result of rearrangement of the 3β-methoxy-epoxide (XIVc).

In contrast to the reactions of the epoxides (XIVd) and (XIVe)[1b,2] the epoxides (XIVa), (XIVb) and (XIVc) give largely products arising from C(5)-O cleavage.

The reluctance of the epoxides (XIVd) and (XIVe) to undergo C(5)-O cleavage was ascribed[1b] to the electron withdrawing nature of the 3β-acetoxy-group. In addition it was suggested[1b] that the unfavourable equatorial to axial conformational change undergone by the 3β-acetoxy-group would hinder the formation of products with the 5β-configuration, from the 5,6α-epoxide (XIVd).

However the conformational free energy differences between equatorial and axial acetoxy-, hydroxy- and methoxy-groups are approximately the same[35] (see table 1). Assuming the effect of co-ordinated boron trifluoride is unimportant, it seems likely that the proposed conformational effect is relatively unimportant in this series, and the electron withdrawing nature of the 3β-substituent (see table 1) [36,37] largely controls the competition between C(5)-O cleavage and fluorohydrin formation.

SUBSTITUENT X	"A"VALUE[29] $k.cal.mole^{-1}$	$\sigma^{*(30,31)}_{-CH_2X}$
F	0.25	+ 1.10
Cl	0.4	+ 1.05
OAc	0.7	+ 0.90[31]
OH	0.7	+ 0.555
OMe	0.7	+ 0.520
H	-	+ 0.490

TABLE 1

Hartshorn and his co-workers recently reported that whereas the 3α-acetoxy-5,6α-epoxide (XIVf) gave essentially products arising from C(5)-O cleavage,[38] the 3α-hydroxy--5,6α-epoxide (XIVg) gave a moderately good yield of fluorohydrin (XVc) (47%).[32] These results show the reverse trend to those described above. Hydrogen bonding as shown (XXV) could assist the formation of the fluorohydrin from compound (XIVg).

Conformational opposition to C(5)-O cleavage by a 3β-substituent implies that the reaction has some degree of concerted character. If the reaction is completely carbonium ion in character, the initially formed reactant like carbonium ion (XXVI) involves no distortion of the A-ring and conformational opposition to its formation would not be expected. The direct formation of a product like carbonium ion e.g. (XXVII) from the initial rate determining C(5)-O cleavage is energetically unfavourable[3] but cannot be

completely ruled out.

If the inductive effect of the 3β-substituent were the only factor governing the competition between C(5)-O cleavage and fluorohydrin formation then the 3β-fluoro-5,6α-epoxide (XIVi)[39] should give a high yield of the fluorohydrin (XVd) when treated with boron trifluoride. A preliminary investigation of this reaction has shown (by t.l.c.) that the epoxide (XIVi) gives a complex mixture with no single major product. However, it will be necessary to look at this reaction in greater detail before the significance of the results can be accurately assessed.

Some of this work has recently been reported by us in the literature.[40]

Discussion 2:-

3β-Acetoxy-5,6α-epoxy-5α-androstan-17-one (XXVIIIa)[41]

when treated with boron trifluoride in benzene gave a mixture.

Preparative t.l.c. of the mixture gave recovered epoxide

(XXVIIIa) (6.5%), the fluorohydrin (XXIXa)[122] (68%) and

the Westphalen derivative (XXXa) (17.5%).

The Westphalen derivative was purified as its diacetate

(XXXb) and was readily identified from its ^{1}H n.m.r. and u.v.

spectra. The former showed the 5β-methyl signal at τ 8.76,

the 13β-methyl signal at τ 9.08 and the 6β-proton as a

quartet (J (apparent) 11 Hz. and 4 Hz.) at τ 5.32.[12,18]

The latter showed an intense end absorption ($\varepsilon_{215\ nm.}$ 5,380).

[19]   Hydrolysis of (XXXb) and oxidation gave the known

3,6-diketone (XXXc).[42]

The crude reaction mixture from 5,6α-epoxy-3β-hydroxy-

5α-androstan-17-one (XXVIIIb)[41] was acetylated and

separated by preparative t.l.c. to give the Westphalen

derivative (XXXb) (35%) and a second fraction, an

inseparable mixture of three products, the fluorohydrin

(XXIXa) (25%), the ketone (XXXIa) (18.5%) and the epoxide

(XXVIIIa) (2.2%). The percentages of the three components

were estimated from the integrated intensities of their

characteristic methine proton signals in the ^{1}H n.m.r.

of the mixture. A sample of the pure fluorohydrin (XXIXa)

was separated by preparative t.l.c..

A sample of the mixture when treated with base

gave a mixture of two products. This was treated with

XXVIII

	R	
(a)	5,6α	Ac
(b)	5,6α	H
(c)	5,6β	H
(d)	5,6α	Me

XXIX

	R	R¹	R²
	R	R^1	R^2
(a)	βOAc,H	OH	βF,H
(b)	βOH,H	OH	βOH,H
(c)	βOH,H	F	βOH,H
(d)	βOAc,H	F	βOAc,H
(e)	βOMe,H	OH	βF,H

XXX

	R	R^1
(a)	βOAc,H	αOH,H
(b)	βOAc,H	αOAc,H
(c)	=O	=O
(d)	βOMe,H	αOAc,H

XXXI

		R
(a)	5β	Ac
(b)	5α	H
(c)	5β	Me
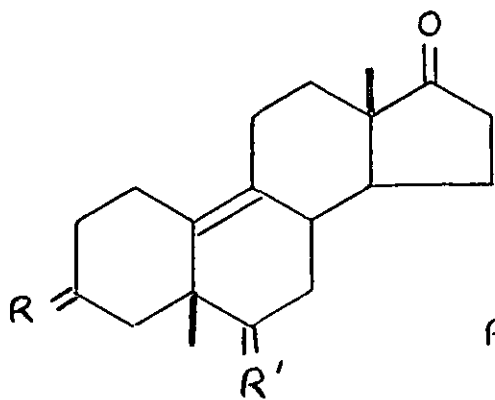
XXXII

	R
(a)	βOAC,H
(b)	=O

periodic acid in acetone,[43] and gave, after preparative

t.l.c., the 6-ketone (XXXIb),[44] confirming the presence

of the ketone (XXXIa) in the original mixture, and the

3β,5α,6β-triol (XXIXb).[45]

Preparative t.l.c. of the reaction mixture obtained from

5,6β-epoxy-3β-hydroxy-5β-androstan-17-one (XXVIIIc)[41]

gave three fractions. The first, an inseparable polar

mixture (20%) was not further investigated. Preparative

t.l.c. of the second fraction gave the ketone (XXXIb)

(15%) and the fluorohydrin (XXIXc) (36%) purified and

identified as its diacetate (XXIXd). Treatment of the

fluoro-compound (XXIXd) with base gave the epoxide (XXVIIIc).

The presence of the tertiary fluorine was indicated by the

mass spectrum (see table), the parent ion (m/e 408)

losing both one and two moles of acetic acid (m/e 348,

288) followed by the loss of hydrogen fluoride (m/e 328,

268 respectively).

The third, minor, fraction was acetylated and purified

by t.l.c. to give a compound tentatively formulated as

(XXXIIa) (6.5%). The ^{1}H n.m.r. spectrum indicated the

presence of a 5β-methyl group (τ 8.75) and a 1,10-double

bond (τ 4.67) by comparison with the spectrum of (XXXb)

(5β-methyl at τ 8.76). The chemical shift of the

13β-methyl (τ 9.11) is not consistent with a $\triangle^{9,11}$-

or $\triangle^{14,15}$- structure.[46] Hydrolysis of (XXXIIa)

followed by oxidation, gave the diketone (XXXIIb).

The ^{1}H n.m.r. spectrum exhibited signals at τ 4.5

(W$\frac{1}{2}$, 12 Hz.), τ 8.76 and τ 9.12 assigned to the olefinic

proton, the 5β-methyl and the 13β-methyl groups respectively.

The i.r. spectrum of (XXXIIb) showed carbonyl bands at

1745 cm.$^{-1}$ and 1720 cm.$^{-1}$. The u.v. spectrum showed the

absence of an α,β-enone, thus eliminating the possibilities

of $\triangle^{4,5}$- or $\triangle^{7,8}$-structures. Snatzke[47] has

reported the base catalysed isomerisation of a $\triangle^{1,10}$-3-ketone

to the α,β-enone. However, treatment of the diketone (XXXIIb)

under the same conditions gave no change in the u.v. spectrum.

5,6α-Epoxy-3β-methoxy-5α-androstan-17-one (XXVIIId)

was prepared from 3β-methoxy-androst-5-en-17-one[48] by

monoperphthalic acid oxidation. The 5,6α-stereochemistry

was readily assigned from the ^{1}H n.m.r. spectrum of (XXVIIId),

the C(6)-methine appearing as a doublet (J (apparent) 4 Hz.)[49]

The reaction mixture from treatment of the epoxide

(XXVIIId) with boron trifluoride was separated by preparative

t.l.c. to give two fractions. These were acetylated and

further separated by t.l.c. and gave the Westphalen derivative

(XXXd) (20%), the ketone (XXXIc) (21%), the fluorohydrin

(XXIXe) (13.5%) and the epoxide (XXVIIId) (4.2%). The

Westphalen derivative (XXXd) was readily identified by a

comparison of its ^{1}H n.m.r. spectrum with that of (XXXb).

The u.v. spectrum of (XXXd) showed a strong end absorption

($\varepsilon_{215 \text{ n.m.}}$ 4,600) confirming the presence of the 9,10-double

bond.[19].

The ketone (XXXIc) was identified from its i.r.spectrum
(1750, 1715 cm.$^{-1}$) and ^{1}H n.m.r. spectrum. The <u>cis</u>-A,B-ring
junction was confirmed by the equatorial 3α-proton (τ 6.59,
$W\frac{1}{2}$ 8 Hz.). The 10β- and 13β-methyl group signals appeared
as a singlet (τ 9.14). This was consistent with the
calculated values for the angular methyl signals of compound
(XXXIc).[46] The fluorohydrin (XXIXe) was readily identified
from its ^{1}H n.m.r. spectrum. Doublets at τ 5.71 (J_{HF} <u>ca</u>.50.
Hz.) and τ 8.87 (J_{HF} 5. Hz.) were observed due to coupling
of the 6β-fluorine atom with the 6α-proton and 10β-methyl
group respectively.[50] The hydroxyl bands (3610, 3400 cm.$^{-1}$)
in the i.r. spectrum confirmed the presence of the 5α-hydroxyl
group. The mass spectrum (see table) and analytical data
supported the proposed structure (XXIXe).

The mixture derived from the reaction of boron trifluoride
etherate with 3β-acetoxy-5,6α-epoxy-5α-pregnan-20-one (XXXIIIa)
[41] was separated by preparative t.l.c. to give the fluoro-
hydrin (XXXIVa)[14] (76%), the Westphalen derivative
(XXXVa) (8.5%) and the epoxide (XXXIIIa) (13%). The
Westphalen derivative was purified as its diacetate (XXXVb)
and was readily identified from its ^{1}H n.m.r.[12,18] and
u.v. spectra.[19]

Hydrolysis and oxidation of (XXXVb) gave the known
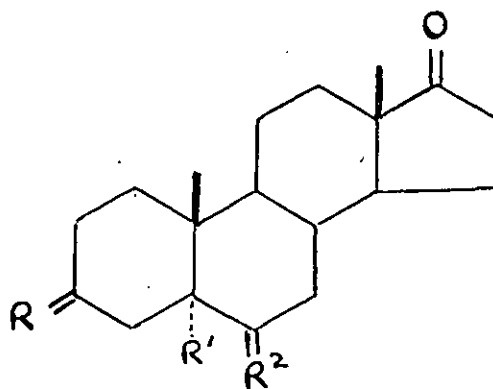diketone (XXXVc);[51] confirming the assigned structure.

The reaction mixture from 5,6α-epoxy-3β-hydroxy-5α-
-pregnan-20-one (XXXIIIb)[41] was acetylated and separated
by preparative t.l.c. and gave the fluorohydrin (XXXIVa)
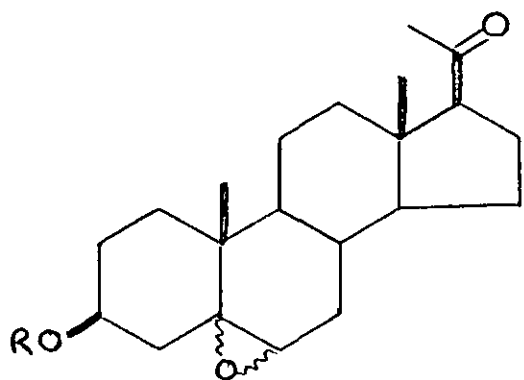
XXXIII

		R
(a)	5,6α	Ac
(b)	5,6α	H
(c)	5,6β	H
(d)	5,6α	Me
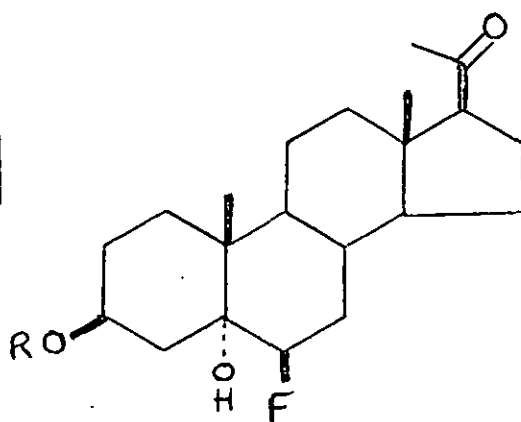
XXXIV

	R
(a)	Ac
(b)	Me

XXXV

	R	R^1
(a)	βOAc,H	αOH,H
(b)	βOAc,H	αOAc,H
(c)	=O	=O
(d)	βOMe,H	αOAc,H
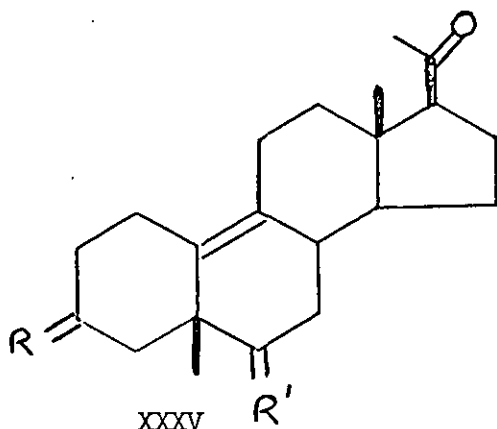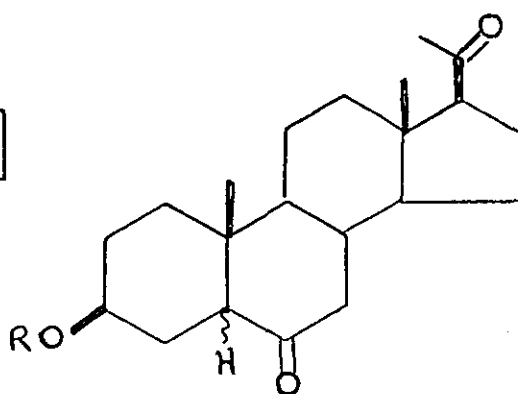
XXXVI

		R
(a)	5β	Ac
(b)	5α	Ac
(c)	5β	Me
(d)	5α	H
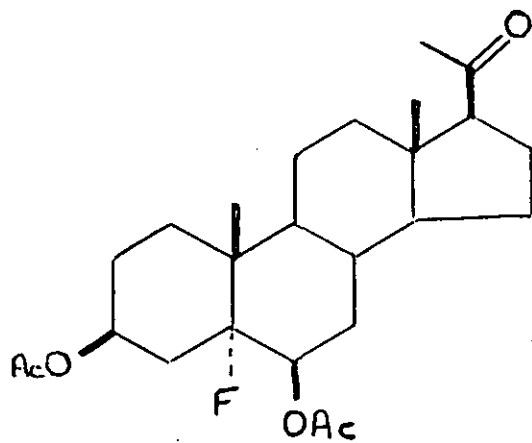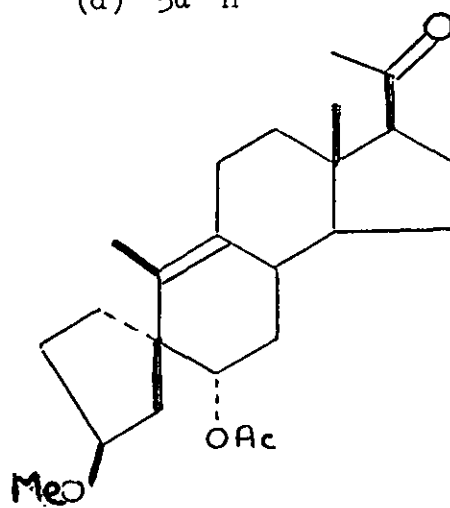
XXXVII

XXXVIII

(9%), the Westphalen derivative (XXXVb) (37%) and the ketone (XXXVIa) (31%). The ketone (XXXVIa) was identified from its ^{1}H n.m.r. spectrum. The 5β-stereochemistry was indicated by the equatorial C(3)-proton (τ 5.02, W$\frac{1}{2}$. 8 Hz.). The 10β-methyl signal (τ 9.14) and 13β-methyl signal (τ 9.44) were also consistent with the assigned structure.[46] The ketone previously reported by Mihina[52] as (XXXVIa) is in fact (XXXVIb). This follows from its mode of preparation (under basic conditions), and by comparison with the original literature.[53]

The reaction mixture from 5,6β-epoxy-3β-hydroxy-5β--pregnan-20-one (XXXIIIc)[41] was acetylated and separated by preparative t.l.c. to give the fluorohydrin (XXXVII) (62.5%) and the ketone (XXXVIb)[53] (26%). The fluorohydrin (XXXVII) was readily identified from its analytical and spectral data. The presence of a 5α-fluorine atom was confirmed by the mass spectrum (see table) in which the parent ion (m/e 436) lost acetic acid (m/e 376) followed by hydrogen fluoride (m/e 356).

5,6α-Epoxy-3β-methoxy-5α-pregnan-20-one (XXXIIId) was prepared by monoperphthalic acid oxidation of 3β-methoxy--pregn-5-en-20-one.[54] The 5,6α-stereochemistry of (XXXIIId) was supported by the ^{1}H n.m.r. spectrum in which the C(6)-proton appeared as a doublet (τ 7.25, J (apparent) 4 Hz.).[49]

Preparative t.l.c. of the mixture obtained from the

epoxide (XXXIIId) gave two fractions. The first fraction was further separated by t.l.c.; the components were acetylated, and again subjected to t.l.c., to give the Westphalen derivative (XXXVd) (23%), the fluorohydrin (XXXIVb) (8%) and the spiro-compound (XXXVIII) (3.5%). The second fraction on preparative t.l.c. gave the ketone (XXXVIc) (13.5%) and the spiro-compound (XXXIX).

The Westphalen derivative (XXXVd) was readily identified from its ^{1}H n.m.r., by comparison with that of (XXXVb), and from the intense end absorption in its u.v. spectrum ($\mathcal{E}_{215\ nm.}$ 5,200).[19] The fluorohydrin (XXXIVb) was readily identifiable from the characteristic proton to fluorine spin-spin coupling constants observed for the 6α-proton (J_{HF} 50 Hz.) and 10β-methyl group (J_{HF} 5 Hz.).[50] The i.r. spectrum (3600, 3450 cm.$^{-1}$) confirmed the presence of the tertiary hydroxyl group.

The u.v. spectrum ($\mathcal{E}_{215\ nm.}$ 6,520) of the spiro-compound (XXXVIII) indicated the presence of a tetrasubstituted olefinic bond.[19] The methyl group appeared as a broad singlet (τ 8.32) in the ^{1}H n.m.r. spectrum, owing to allylic coupling. The 13β-methyl group (τ 9.31) and 6β-methine proton (τ 5.33, J (apparent) 11 Hz., 4 Hz.) confirmed the 9,10-position of the double bond by comparison with the ^{1}H n.m.r. spectrum of (XXXVd). The C(5) stereochemistry was assigned on mechanistic considerations.

The 5β-stereochemistry of the ketone (XXXVIb) was
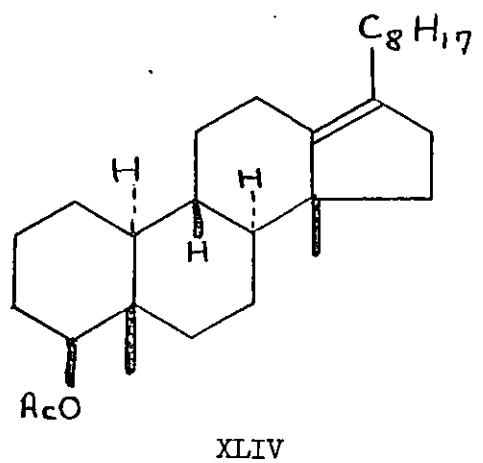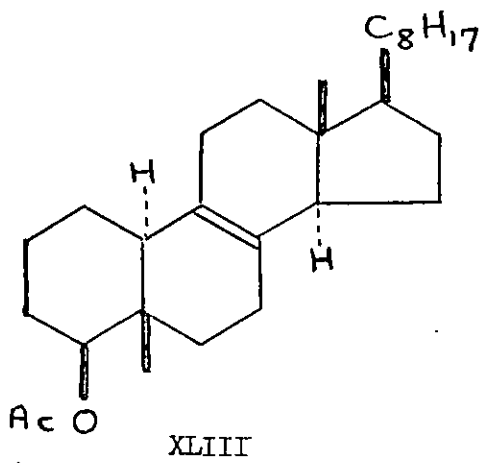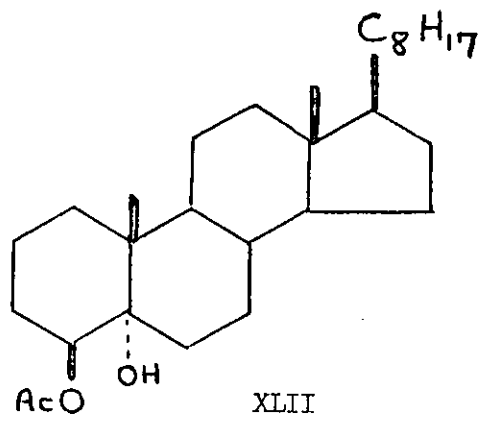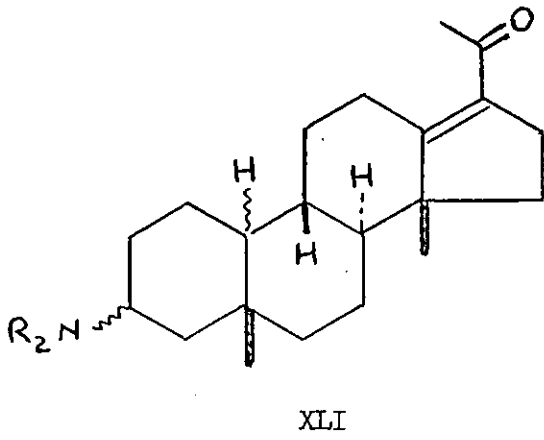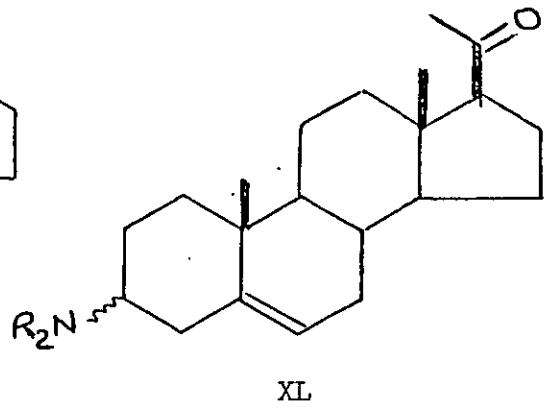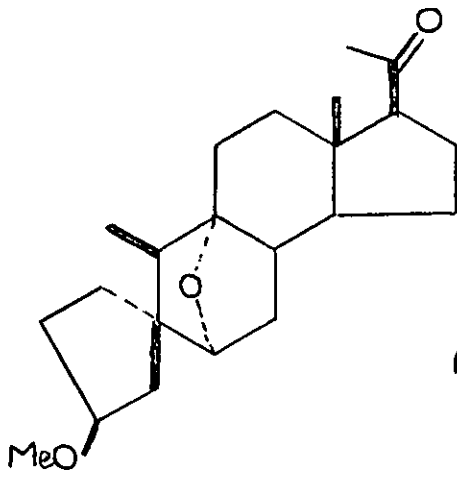
XXXIX

XL

XLI

XLII

XLIII

XLIV

indicated by the equatorial 3α-proton (τ 6.58 ($W\frac{1}{2}$, 8 Hz.)).

The 13β- and 10β-methyl signals (τ 9.42, 9.19 respectively)

also agreed with the proposed structure.[46]

The structure was assigned to the compound (XXXIX)

essentially by comparison of its [1]H n.m.r. spectrum with

that of the compound (XXII) (see also Discussion 3).

Analytical data and the mass spectrum (see table) showed

it was isomeric with compound (XXXIIId). The i.r. spectrum

of compound (XXXIX) showed no hydroxyl band.

The 100 M.Hz. [1]H n.m.r. spectrum of compound (XXXIX)

showed a doublet (J _ca_. 6 Hz.) at τ 6.17 assigned to the

6β-proton. The 10-methyl group gave rise to a doublet

(J _ca_. 7.5 Hz.) at τ 9.15. Double irradiation 66 Hz.

downfield from the 10-methyl doublet caused its collapse

to a singlet.

The preceding results show that, as with the cholestane

5,6α-epoxides (XIV d,a,e), variation of the 3β-substituent

from acetoxyl to hydroxyl and methoxyl in the 5α-androstan-

-17-one 5,6α-epoxides (XXXVIIIa,b,d) and 5α-pregnan-20-

-one 5,6α-epoxides (XXXIIIa,b,d) produces a reduction in

the yields of their respective fluorohydrins and an increase

in the percentage of products derived from C(5)-O cleavage.

However, the reduction in yields of the fluorohydrins are

not as great in the latter two series as in the cholestane

series. This may be due to the operation of long range

effects destabilising the formation of a C(5)-carbonium

ion (A_1 type mechanism) relative to fluorohydrin formation (A_2 type mechanism). Long range conformational, electro-static and inductive effects have been reviewed recently.[55] It is not clear which of these effects (or combination of these) operates in this case. If the yields of the isolated fluorohydrins are accurately representative, then for a given 3β-substituent the decrease in yield of the fluoro-hydrins on progressing from the androstan-17-one through the pregnan-20-one to the cholestane series of epoxides can be qualitatively equated with the expected reduced inductive (-I) effect felt at C(5) from the C(17)-substituents.[36] A more quantitative approach is necessary however to provide definite evidence on which effects operate.

The effect of ring D and its substituents on the fate of the C(5) carbonium ion, once formed, i.e. the ratio of products derived from 10β-methyl migration to other products, cannot be assessed from the above results. However, Crastes de Paulet[56] has suggested such an effect would operate.

It has been found that the olefins (XL) can be rearranged to the "backbone" products (XLI)[57] demonstrating the feasibility of such rearrangements with a 17β-acetyl substituent. The 5α-pregnan-20-one epoxides (XXXIIIa,b,d) gave no such backbone rearranged compounds. However, the compound (XXXIX) isolated from the epoxide (XXXIIId)

does arise from a C(9) carbonium ion. It would therefore appear that the combined presence of the C(6α)-O$\overset{O}{B}$F$_3$ and the 17-CH$_3$CO groups prevent the formation of a C(8) carbonium ion. Electronegative groups at C(6) have recently been shown to inhibit C(8) carbonium ion formation. For example, the hydroxy-steroid (XLII) gives the olefins (XLIII) (14%) and (XLIV) (3%) under the conditions of the Westphalen rearrangement.[58] The efficiency of the backbone rearrangement from some 10β-hydroxy-steroids has also been found to be susceptible to C(6) electronegative substituents.[59]

Discussion 3:-

Having investigated the sensitivity of the boron trifluoride-
catalysed opening of some 5,6-epoxides with variations in the
3β-substituent it was decided to determine whether these
reactions are sensitive to changes in C(19)-substituents.
It was felt that some C(19)-methyl-epoxides (XLV) would
provide the simplest system for an initial study. In such
a system the change in electronic effects from the 10β-
substituent would be minimised, allowing a study of any
conformational or steric effects operating. This system
(XLV) would also provide a useful parallel to the work on
the Westphalen rearrangement of C(19)-substituted steroids
which was being undertaken in these laboratories at
the time.[60a,b]

The C(19)-oxo-compound (XLVI) was prepared as
described in the literature.[61] Treatment of the compound
(XLVI) with methylenetriphenylphosphorane in dry benzene
gave the diene[60a] (XLVII) (69%). Selective hydrogenation
of the diene (XLVII) with a palladium-charcoal catalyst gave
the C(19)-methyl compound (XLVIIIa). A single vinylic
proton signal (τ 4.55, W$\frac{1}{2}$ ca. 9 Hz.) in the [1]H n.m.r.
spectrum confirmed that reduction of the 10β-ethenyl group
had occurred. Oxidation of the olefin (XLVIIIa) with
monoperphthalic acid gave the α-epoxide (XLVa) selectively.
The stereochemistry of the epoxide was confirmed by the
[1]H n.m.r. spectrum in which the 6β-methine proton
appears as a doublet (J 3.1 Hz.).[49] Acetylation of the
compound (XLVa) using acetic anhydride in pyridine gave
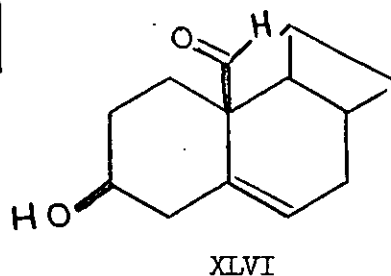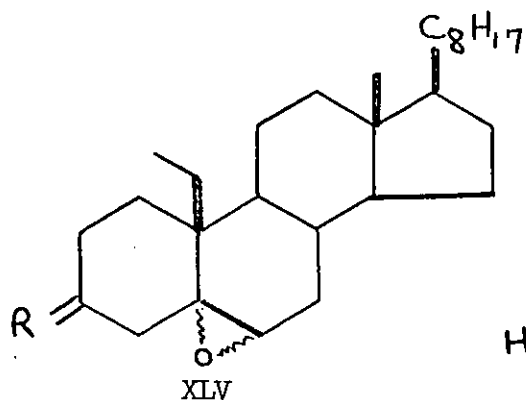
XLV

XLVI

R
(a) 5,6α βOH,H
(b) 5,6α βOAc,H
(c) 5,6α βOMe,H
(d) 5,6α αOAc,H
(e) 5,6β αOAc,H
(f) 5,6α αOH,H
(g) 5,6β αOH,H
(h) 5,6β βOAc,H
(i) 5,6β βOH,H

XLVII

XLVIII
R
(a) βOH,H
(b) βOMe,H
(c) αOAc,H

XLIX
R
(a) H
(b) MeSO₂-

L

	R	R¹	R²
(a)	H	H	-CHO
(b)	H	H	H
(c)	Ac	Ac	Ac
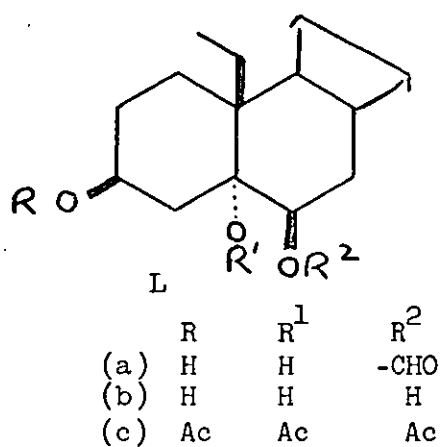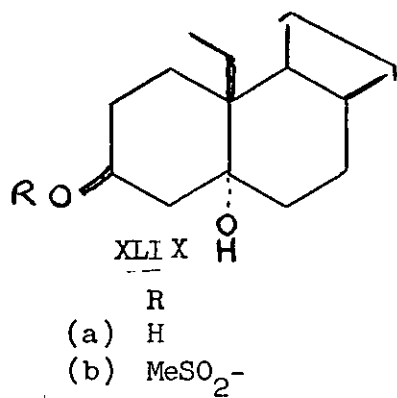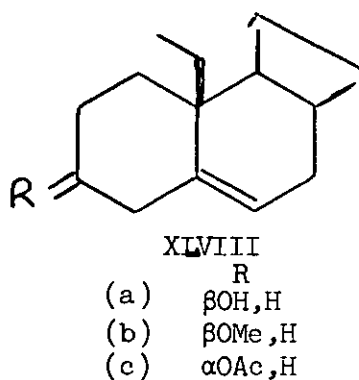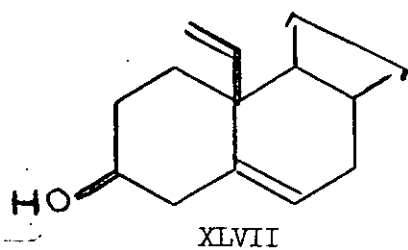
the epoxide (XLVb).

3β-Methoxy-19-methyl-cholest-5-ene (XLVIIIb)[60b] was

prepared by treatment of 19-methyl-cholesterol (XLVIIIa)

with perchloric acid in trimethylorthoformate.[62] Oxidation

of the compound (XLVIIIb) with monoperphthalic acid gave

the 5,6α-epoxide (XLVc) selectively. The 5α,6α-stereochemistry

was confirmed by the [1]H n.m.r. [49] spectrum (cf. XLVa).

The epoxide (XLVa) was reduced with lithium aluminium

hydride in ether to give the 3β,5α-diol (XLIXa) (68%).

This, on treatment with methane sulphonyl chloride in

pyridine, gave the 3β-mono-mesylate (XLIXb) quantitatively.

The mesylate (XLIXb) was refluxed with acetyl chloride in

1:1 chloroform/diethylaniline.[63] Column chromatography

of the crude reaction product gave pure 3α-acetoxy-19-methyl-

cholest-5-ene (XLVIIIc) (45%).

The [1]H n.m.r. spectrum of the compound (XLVIIIc) showed

signals for the expected 3β-equatorial methine proton ($W_{\frac{1}{2}}$.,

9 Hz.), the olefinic proton (τ 4.58), and the 3α-acetoxy

group (τ 8.08).

Epoxidation of the olefin (XLVIIIc) with monoperphthalic

acid gave a mixture which was separated by preparative t.l.c.

to give the 5,6α-epoxide (XLVd) (32%) and the 5,6β-epoxide

(XLVe) (38%).

The spin-spin coupling patterns and chemical shifts

observed for the C(6) protons in the [1]H n.m.r. spectra of

compounds (XLVd) (τ 7.40, d, J ca. 3 Hz.) and (XLVe) (τ 7.31

in $W_{\frac{1}{2}}$ ca. 4 Hz.) allowed the assignment of the epoxide stereochemistry

in each case.[49] The mass spectra (see table) and analytical

24.

data for compounds (XLVd) and (XLVe) also supported the assigned structures. Hydrolysis of the two epoxides (XLVd) and (XLVe) gave the 3α-hydroxy-epoxides (XLVf) and (XLVg) respectively.

19-Methyl-cholesterol (XLVIIIa) was treated with performic acid to give the 5α-hydroxy-6β-formate (La) which was hydrolysed to give the triol (Lb). Reaction of the triol (Lb) with acetic anhydride and p-toluenesulphonic acid gave the triacetate (Lc). The triacetate (Lc) was refluxed with ethanolic potassium hydroxide and the crude reaction mixture re-acetylated using acetic anhydride in pyridine. Column chromatography of this mixture gave the 5β,6β-epoxide (XLVh) (40%). The mass spectrum (see table), analytical data and ^{1}H n.m.r. spectrum (C(6α)-H, τ 7.14 W$\frac{1}{2}$ ca. 4Hz.) supported the structure (XLVh). Hydrolysis of the epoxide (XLVh) gave the epoxide (XLVi). The ^{1}H n.m.r. spectra of the α-epoxides (XLVa,b,c,d,f) all show a 6β-proton-7β-proton coupling constant of ca. 3.1 Hz. This is smaller than that observed for normal 10β-methyl-5,6α-epoxides[49] (J 3.7-4.8 Hz.).

The most stable conformation for the ethyl group in the epoxides (XLVa,b,c,d,f) is probably close to that represented in (LI). The 10β-ethyl group suffers an interaction with the 11β-hydrogen atom and 1,3-interactions with the syn-2β,-4β,- and 8β-hydrogen atoms. These interactions being greater than those for a 10β-methyl group
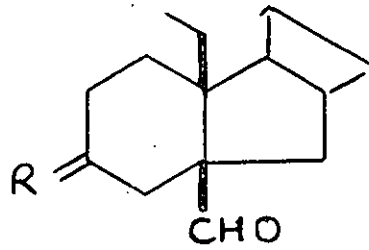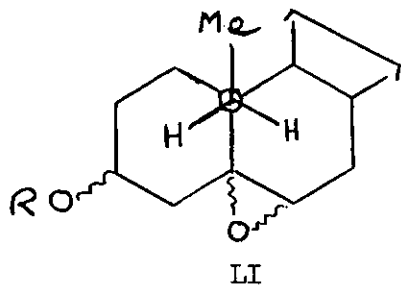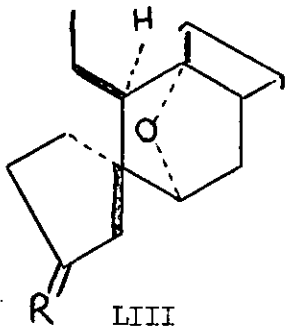
LI

LII

R

(a)   βOAc,H
(b)   αOAc,H

LIII

R

(a)   βOAc,H
(b)   βOH,H
(c)   =O
(d)   βOMe,H
(e)   αOAc,H

LIV

LV

R

(a)   5β   βOAc,H
(b)   5β   βOMe,H
(c)   5α   βOAc,H
(d)   5β   αOAc,H
(e)   5α   αOAc,H

LVI

R   R¹
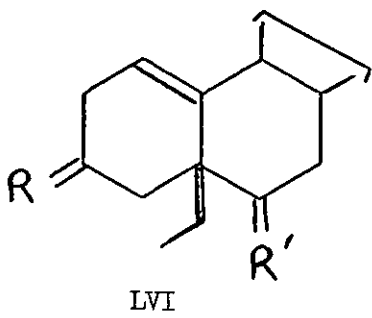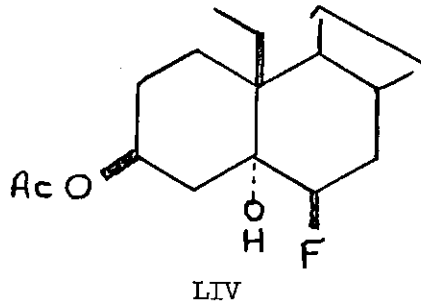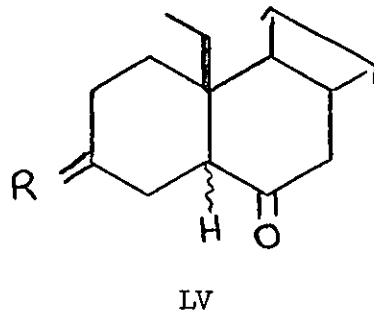
(a)   βOAc,H   αOAc,H
(b)   =O   =O
(c)   βOH,H   αOH,H

probably cause some flattening of the A-and B-rings and possibly the C-ring. This would cause the 7-carbon atom to rotate towards the β-face of the molecule. The 6β-proton-7β-proton dihedral angle would increase and thus lead to the reduced spin-spin coupling constant which is observed. For the β-epoxides (XLVe,g,h,i), this flattening would increase the 6α-proton-7β-proton dihedral angle and decrease the 6α-proton-7α-proton dihedral angle. The coupling constant for the latter would increase while that for the former would decrease, thus causing the normally observed narrow doublet[49] (J 2.1-2.7 Hz.) to become an unresolved multiplet in the β-epoxides (XLVe,g,h,i).

The epoxide (XLVb) was treated with boron trifluoride in benzene, and the reaction mixture separated by preparative t.l.c., to give three fractions. Further t.l.c. of one of these gave the aldehyde (LIIa) (13%) and the ether (LIIIa) (3%). Acetylation and preparative t.l.c. of the remaining fractions gave the fluorohydrin (LIV) (19%), the ketone (LVa) (19%), the olefin (LVIa) (3.5%), the Westphalen derivative (LVIIa) (15%), the backbone-rearranged compound (LVIIIa) (3%) and the spiro-compound (LIXa) (3%).

The fluorohydrin (LIV) was readily identified from spectroscopic data. The ^{1}H n.m.r. spectrum shows the C(6)--methine proton as a doublet (J_{HF} ca. 49 Hz.). The i.r. spectrum confirms the presence of the tertiary hydroxyl group (3440 cm.$^{-1}$). Identification was confirmed by the conversion

26.
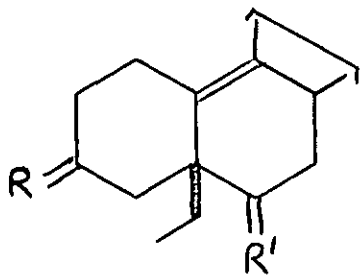
LVII

	R	R^1
(a)	βOAc,H	αOAc,H
(b)	=O	=O
(c)	βOMe,H	αOAc,H
(d)	βOMe,H	=O
(e)	αOAc,H	αOH,H
(f)	αOAc,H	αOAc,H
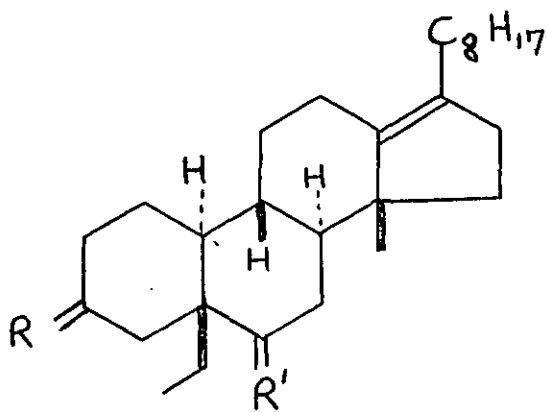
LVIII

	R	R^1
(a)	βOAc,H	αOAc,H
(b)	=O	=O
(c)	βOAc,H	βOH,H
(d)	αOAc,H	αOH,H
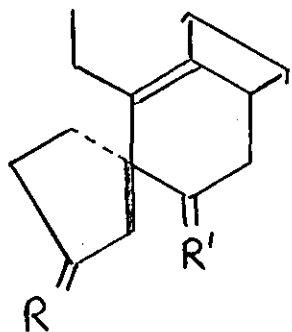
LIX

	R	R^1
(a)	βOAc,H	αOAc,H
(b)	=O	=O
(c)	βOMe,H	αOAc,H
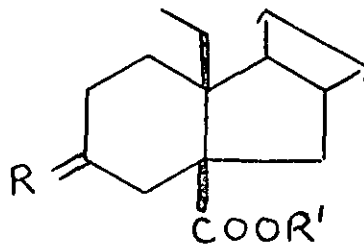
LX

	R	R^1
(a)	βOH,H	H
(b)	βOH,H	CH$_3$
(c)	αOH,H	H
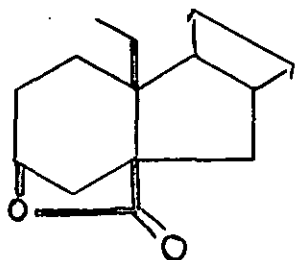
LXI
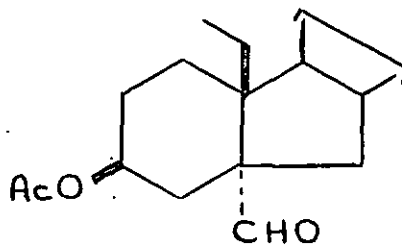
LXII

of the fluorohydrin (LIV) to the epoxide (XLVa) with methanolic

potassium hydroxide. The ketone (LVa) was identified from its

i.r. spectrum (1740, 1710 cm.$^{-1}$). The 5β-configuration of the

ketone (LVa) was confirmed by the ^{1}H n.m.r. spectrum which

showed an equatorial C(3)-proton (W$\frac{1}{2}$., ca. 8 Hz.).

The structure of the olefin (LVIa) was tentatively

assigned on the following spectroscopic evidence. The ^{1}H n.m.r.

spectrum of the compound (LVIa) shows the 13β-methyl group

(τ 9.30) and an olefinic proton (τ 4.75). The chemical

shift of the 13β-methyl group excludes the possibility of

$\triangle^{9,11}$- or $\triangle^{14}$-structures,[46] and is consistent with the

observed chemical shifts (τ 9.30 - 9.32) of 13β-methyl groups

in other $\triangle^{1,10}$-compounds.[60a] Hydrolysis and oxidation

of compound (LVIa) gave the diketone (LVIb) which shows no

α,β-enone absorption in its u.v. spectrum, excluding $\triangle^{4}$- or

$\triangle^{7}$ - structures.Attempted base catalysed isomerisation

of the compound (LVIb)[47] gave a complex mixture which was

not further investigated (c.f. compound (XXXIIb)).

The chemical shift of the 13β-methyl group (τ 9.2) in

compound (LVIIa) is typical of $\triangle^{9}$-compounds.[12] The

triplet due to the methyl portion of the 5β-ethyl group

appears at τ 9.30. Strong end absorption ($\epsilon_{215\ nm.}$ 5,300)

in the u.v. spectrum of compound (LVIIa) indicates the

presence of a 9,10-double bond.[19] Hydrolysis and oxidation

of the diacetate (LVIIa) gave the diketone (LVIIb)

($\epsilon_{215\ nm.}$ 5,600). The i.r. spectrum shows a carbonyl band

at 1725 cm.$^{-1}$ The chemical shift of the methyl triplet of

the 5β-ethyl group in compound (LVIIb) (τ 9.46) is similar

to that previously observed for a 5β-ethyl-6-oxo- Δ^9-compound.[60a]

The $\Delta^{13,17}$-compound (LVIIIa) was identified from its

^{1}H n.m.r. spectrum.   The C(21)H$_3$-doublet appears at τ 9.05

(J ca. 6 Hz.).   Double irradiation 88 Hz. downfield from

the doublet caused its collapse.[2]   The mass spectrum (see

table) of the olefin (LVIIIa) shows an intense and characteristic[22]

peak at m/e 387, corresponding to loss of side chain. Hydrolysis

and oxidation of the diacetate (LVIIIa) gave the diketone (LVIIIb).

The i.r. spectrum shows a carbonyl absorption at 1720 cm.$^{-1}$

The ^{1}H n.m.r. spectrum of the spiro-compound (LIXa)

appears to be that of a typical Westphalen compound.   The

13β-methyl signal appears at τ 9.20,[12] and the C(6) methine

appears as a quartet (τ 5.28, J(apparent) 11 Hz., 4Hz.).[18]

Hydrolysis and oxidation of the diacetate (LIXa) gave the

diketone (LIXb).   The i.r. spectrum of the diketone (LIXb)

clearly shows the cyclopentanone (1752 cm.$^{-1}$) and cyclohexanone

(1715 cm.$^{-1}$) systems, confirming the structure of compound

(LIXa).   Low field chemical shifts of 13β-methyl groups in

spiro-compounds of this type have been noted by other

workers.[6,7]   The C(5) stereochemistry was assigned on

mechanistic considerations.

The aldehyde (LIIa) shows the expected singlet

(τ 0.3) in the ^{1}H n.m.r. spectrum for the aldehydic proton.

The i.r. spectrum also confirms the presence of the aldehyde

group (2720, 1720 cm.$^{-1}$).   The signal due to the C(3) proton

(W$\frac{1}{2}$., 13 Hz.) in the ^{1}H n.m.r. spectrum does not allow a

completely unequivocal assignment of the C(5) stereochemistry.

It does indicate a possible 5β-configuration for the aldehyde

(LIIa) in which the A-ring adopts a twist conformation,

possibly to relieve the 1,3-interaction between the 5β-

aldehyde and 3β-acetate groups.   Oxidation of the aldehyde

(LIIa) followed by hydrolysis gave the hydroxy-acid (LXa).

Treatment of the acid (LXa) with a trace of toluene-p-sulphonic

acid in refluxing benzene gave the γ -lactone (LXI) in

high yield (ν $_{max.}$ 1780 cm.$^{-1}$).   The ^{1}H n.m.r. spectrum

shows an equatorial C(3) methine proton (τ 5.5, W$\frac{1}{2}$., ca.

8 Hz.) in support of the chemical evidence for the 5β-aldehyde

group.

The γ -lactone (LXI) was refluxed in methanolic

potassium hydroxide for 6 hr. to give a polar material.

This was treated with diazomethane. Preparative t.l.c.

gave the hydroxy-ester (LXb) (40%). This ester (LXb) was

shown (by t.l.c. and ^{1}H n.m.r. data) to be identical with an

authentic sample obtained directly from the acid (LXa).

The possibility of C(3)-O cleavage occurring during

lactonisation and the alternative structure (LXII) for the

aldehyde can thus be excluded.

The structure of the ether (LIIIa) rests on the

following evidence. The ^{1}H n.m.r. spectrum of the ether

(LIIIa) shows a doublet at τ 6.33 (J. ca., 6 Hz.), assigned

to the C(6) proton. The i.r. spectrum of the compound
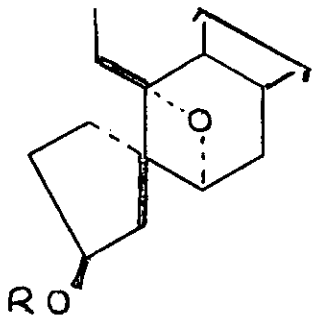
LXIII
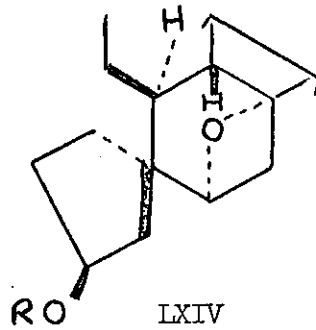
LXIV
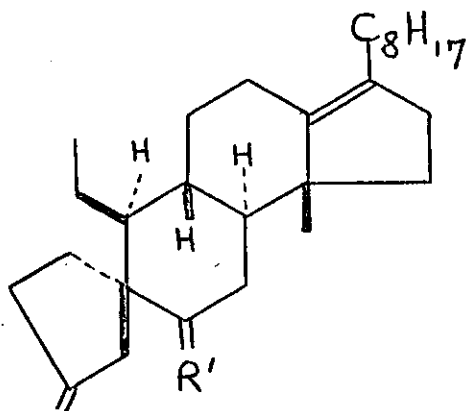
LXV

	R	R^1
(a)	βOAc,H	αOAc,H
(b)	βOH,H	αOH,H
(c)	=O	=O
(d)	αOAc,H	αOAc,H
(e)	αOH,H	αOH,H
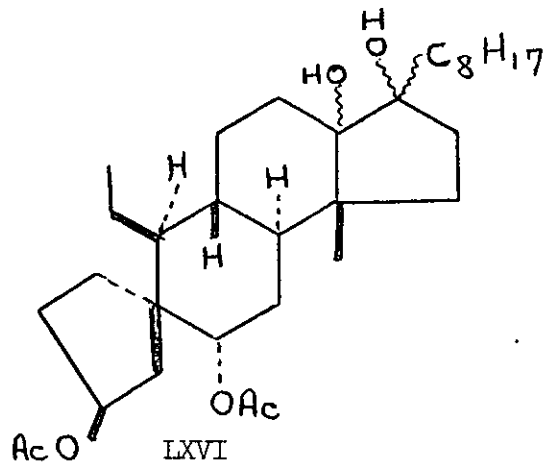
LXVI
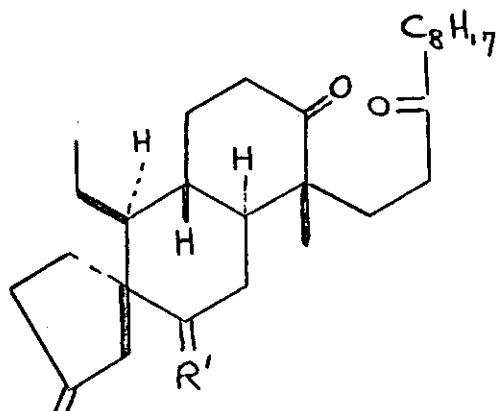
LXVII

	R	R^1
(a)	βOAc,H	αOAc,H
(b)	βOH,H	αOAc,H
(c)	βOH,H	αOH,H
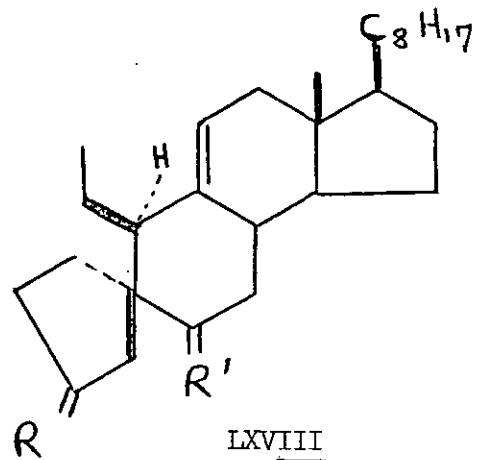
LXVIII

	R	R'
(a)	βOAc,H	αOAc,H
(b)	βOH,H	αOH,H
(c)	=O	=O

(LIIIa) shows no hydroxyl band and suggests the C(6) oxygen

function is an ether. The i.r. spectrum of compound (LIIIb)

shows no carbonyl band. Oxidation of the alcohol (LIIIb)

gave the cyclopentanone (LIIIc) ($\nu_{max.}$ 1740 cm.$^{-1}$).

The ^{1}H n.m.r. spectrum of the ketone (LIIIc) showed the

C(6)-methine proton at τ 6.10 (J. ca. 6 Hz.). An examination

of molecular models showed that the three structures (LIII),

(LXIII) and (LXIV) could each give rise to the observed C(6)-

methine proton doublet. The ^{1}H n.m.r. spectra of the similar

compounds (XXII) and (XXXIX) each show the 10-methyl group as

a doublet excluding the general structure (LXIII).

Attempted reduction of (LIIIb) with lithium aluminium

hydride and with lithium in ethylamine gave recovered starting

material. The unreactive nature of the cyclic ether would

not be expected for a highly strained oxetan such as (LXIII)

or (LXIV), and led to a preference for the structure (LIIIa)

for the ether.

Treatment of the ether (LIIIa) with boron trifluoride in

acetic anhydride[33] gave a single product, the diacetate

(LXVa). The ^{1}H n.m.r. spectrum of the diacetate (LXVa) shows

the C(21)H$_3$-doublet (τ 9.04, J. ca. 6 Hz.) and the 14β-

-methyl group (τ 9.18). Hydrolysis of the diacetate (LXVa)

gave the diol (LXVb). The ^{1}H n.m.r. spectrum of the diol

(LXVb) shows the C(21)H$_3$-doublet (τ 9.04, J. ca. 8 Hz.) and

the 14β-methyl group (τ 9.17). The base peak in the mass

spectrum of the diol (LXVb) (m/e 285) corresponds to the loss

of side chain and water from the molecular ion, confirming

the $\triangle^{13,17}$-structure.[22] Oxidation of the diol (LXVb)

gave the diketone (LXVc). The i.r. spectrum shows carbonyl

bands at 1750 cm.$^{-1}$ and 1715 cm.$^{-1}$ The ^{1}H n.m.r. and mass

spectra again support the assigned $\triangle^{13,17}$ structure.

Treatment of the diacetate (LXVa) with osmium tetroxide

in ether/pyridine gave the cis-glycol (LXVI). The i.r.

spectrum of the compound (LXVI) confirms the presence of the

tertiary hydroxyls (3640, 3500 cm.$^{-1}$). The structure is

also supported by the ^{1}H n.m.r. and mass spectroscopic data.

The glycol (LXVI) was treated with periodic acid to give the

dione (LXVIIa). The ^{1}H n.m.r. of the dione (LXVIIa) shows

the C(21)H$_3$-doublet (τ 9.01, J. ca. 7 Hz.) and the

14β-methyl group (τ 9.01). The mass spectrum shows a

strong peak (m/e 448) corresponding to the loss of side

chain by a McLafferty rearrangement.[64] Hydrolysis of

the dione (LXVIIa) with potassium carbonate gave the hydroxy

acetate (LXVIIb). On further treatment of the mono-acetate

(LXVIIb) with potassium carbonate the diol (LXVIIc) was

obtained. The i.r. spectrum of the diol shows a carbonyl

absorption at 1710 cm.$^{-1}$ consistent with the assigned

structure. The ^{1}H n.m.r. spectrum of the dione (LXVIIc)

shows the C(21)H$_3$-doublet (τ 8.91, 9.04) and the 14β-methyl

group (τ 9.04). Double irradiation 88 Hz. downfield from

the C(21)H$_3$-doublet causes its collapse and confirms that

the C(20) proton is alpha to a carbonyl group.[2] The

mass spectrum of compound (LXVIIc) shows a strong peak (m/e 364) corresponding to loss of side chain from the molecular ion by a McLafferty rearrangement.[64] This was confirmed by accurate mass measurements.

The exclusive formation of the $\triangle^{13,17}$-compound (LXVa) from the ether (LIIIa) lends some support to the proposed structure, since a series of trans-1,2-shifts are possible to give the compound (LXVa). A structure (LXIV) would need the development of a full carbonium ion at C(8) to enable a cis-migration of the 14α-proton to take place. This is probably a less favourable process.

The use of boron trifluoride in acetic anhydride/acetic acid has been reported to reduce the percentage of rearranged products compared to the boron trifluoride in acetic anhydride system.[65] Presumably the presence of a basic species i.e. acetate anion, from the solvent enables elimination, by an E_1 and/or E_2 type mechanism, to compete effectively with the rearrangement. Treatment of the ether (LIIIb) with boron trifluoride/acetic anhydride/acetic acid gave two products. Preparative t.l.c. gave the olefin (LXVa) (45%) and a second olefin (LXVIIIa) (55%). The ^{1}H n.m.r. spectrum of the compound (LXVIIIa) shows an olefinic proton (τ 4.73) and the 13β-methyl group (τ 9.39). The high field position of the 13β-methyl group excludes a $\triangle^{14}$-structure and supports the assigned $\triangle^{9,11}$-structure.[46,66] Hydrolysis of the diacetate (LXVIIIa) gave the diol (LXVIIIb) which was oxidised to give the diketone (LXVIIIc). The

LXIX

LXX

LXXI

LXXII

LXXIII

LXXIV

LXXV

LXXVI
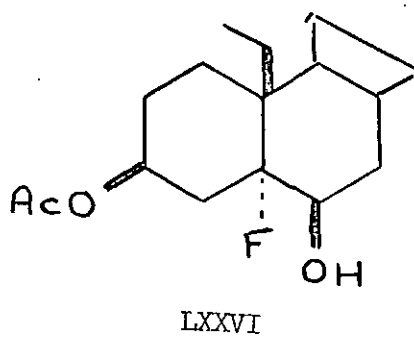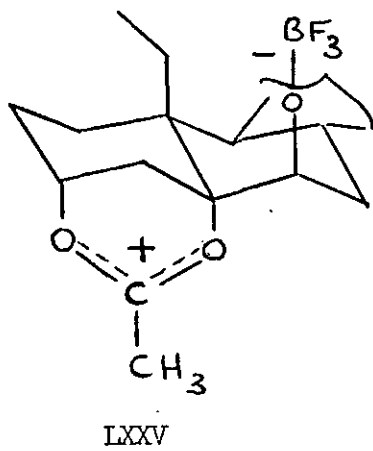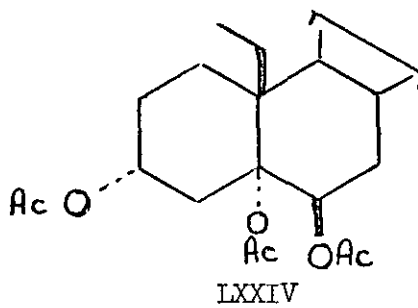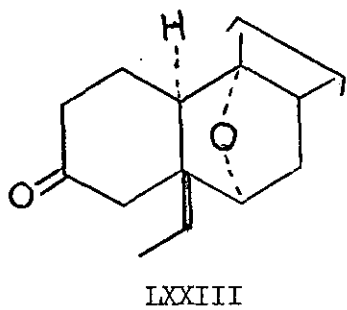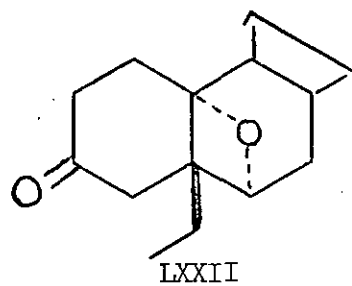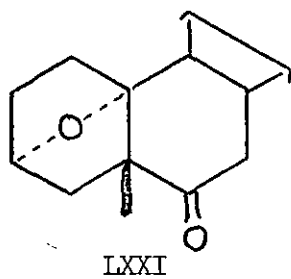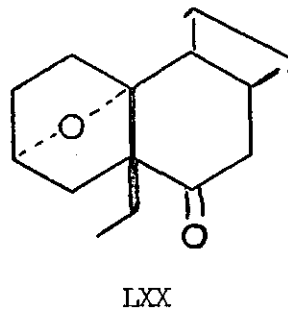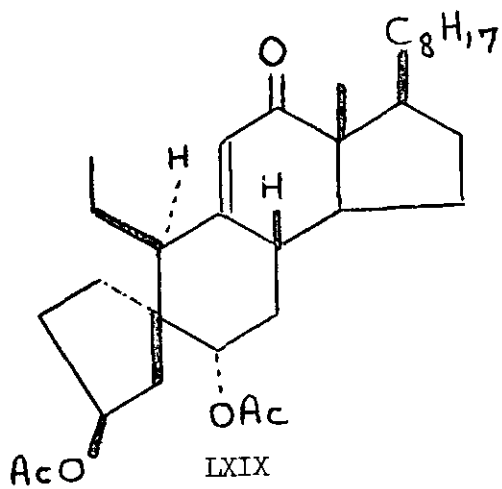
u.v. and i.r. ($\nu_{max.}$ 1755,1715 cm.$^{-1}$)   spectra of the

compound (LXVIIIc) show the absence of an α,β-enone system

and a $\triangle^7$ - structure is thus excluded.

Allylic oxidation of the diacetate (LXVIIIa) using

N-bromosuccinimide in buffered aqueous dioxan[67] gave the

α,β-enone (LXIX).   The i.r. spectrum (1685 cm.$^{-1}$)

indicates an α,β-unsaturated cyclohexanone. This is

confirmed by the u.v. spectrum ($\lambda_{max.}$ 237 nm, $\varepsilon_{max.}$

11,100).   This compares well with data for other

$\triangle^{9,11}$-12-ketones.[68]   The 100 M.Hz. ^{1}H n.m.r. spectrum

of the compound (LXIX) shows the 13β-methyl group at low

field (τ 9.18).   The downfield shift of this methyl group

(0.21 ppm) from that observed for the olefin (LXVIIIa)

is consistent with the introduction of a 12-keto-group.[46]

The vinylic proton (τ 4.35) appears as a doublet (J.ca.

2 Hz.) due to allylic coupling to only one proton.

Examination of a molecular model of compound (LXIX) shows

that a 10α-methine proton has a 0° dihedral angle with the

plane of the olefinic bond and consequently it would not

couple to the olefinic proton.[69]   The 8β-methine proton

in compound (LXIX) has a dihedral angle approaching 90° and

and would be expected to couple with the olefinic proton to

give the observed doublet.[69]   The alternative structure

for compound (LXIX) possessing a 10β-proton can be excluded

since the olefinic proton should appear as a quartet or

triplet. Attempts to isomerise the olefin (LIXb) to olefin

(LXVIIIc) or vice versa using hydrogen bromide in acetic

acid were unsuccessful. Both compounds remained unchanged.
cf.(22,70) Treatment of the olefin (LVIIa) with boron

trifluoride in benzene over an extended period gave no

observable isomerisation to compound (LVIIIa).

The reaction mixture from the 5α,6α-epoxide (XLVa) was

separated by preparative t.l.c. to give four fractions.

The first two fractions were acetylated using acetic anhydride

in pyridine. Further t.l.c. gave the Westphalen compound

(LVIIa) (9%), the spiro-compound (LIXa) (4%), the ketone

(LVa) (13.5%) and the olefin (LVIa) (6.5%). The third

fraction gave the ether (IIIb) (10.5%). The fourth fraction

(25%) proved to be inseparable.

The reaction mixture from the 5α,6α-epoxide (XLVc) was

separated by preparative t.l.c. to give four fractions.

The first two were acetylated and purified by further t.l.c.

to give the spiro-compound (LIXc) (8.3%), the Westphalen

compound (LVIIc) (3%) and the ketone (LVb) (31%). The third

fraction gave the ether (LIIId) (16%). The fourth, non

polar fraction (17%) was not further investigated.

The structure of the spiro-compound (LIXc) is indicated

from its [1]H n.m.r. spectrum in which the 13β-methyl group

appears at τ 9.23,[6,7] and the 6β-methine appears as a quartet

(τ 5.33, J (apparent) $\underline{ca}$. 12 Hz., 4 Hz.). Treatment of

the compound (LIXc) with boron trifluoride in acetic

anhydride gave the spiro-compound (LIXa) (30%). Hydrolysis

and oxidation of (LIXa) to (LIXb) confirmed the assigned structure.

The Westphalen compound (LVIIc) was readily identifiable from its ^{1}H n.m.r. spectrum. The 13β-methyl group appears at ⲧ9.21 and the 6β-methine proton appears as a quartet (ⲧ 5.15, J (apparent) 12 Hz., 4 Hz.).[12,19] In addition the 5β-ethyl group triplet appears at ⲧ9.36 (J. ca. 7 Hz.). Hydrolysis and oxidation of the acetate (LVIIc) gave the known ketone (LVIId)[60a] confirming the assigned structure.

The ketone (LVb) was identified from its i.r. and ^{1}H n.m.r. spectral data. The i.r. spectrum shows a carbonyl band at 1710 cm.$^{-1}$ The ^{1}H n.m.r. spectrum confirms the equatorial conformation for the C(3)-methine proton (W½. 8 Hz.) and the 5β-stereochemistry.

The ^{1}H n.m.r. spectrum of the ether (LIIId) exhibited the expected doublet for the C(6)-methine proton (ⲧ 6.32, J. (apparent) ca. 5 Hz.). The i.r. spectrum confirmed the absence of hydroxyl and keto-groups. Treatment of the ether (LIIId) with boron trifluoride in acetic anhydride gave a mixture, from which the olefin (LXVd) (23%) was separated. The structure (LXVd) was assigned on the basis of the ^{1}H n.m.r. which is similar to that of compound (LXVa). The C(3)-methine (ⲧ 4.94) and C(6)-methine (ⲧ 5.09) protons of compound (LXVd) resonate at a slightly lower field than those of compound (LXVa) (C(3); ⲧ 4.99; C(6),ⲧ5.32). A slight downfield shift in the -OAc signals of compound (LXVd) is also observed. Hydrolysis of the diacetate (LXVd) gave the diol (LXVe). The mass spectrum (see table) of the compound (LXVe) shows

intense peaks (m/e 285 and m/e 267) corresponding to the loss

of side chain and one or two molecules of water from the

molecular ion (m/e 416). These intense peaks support the

$\triangle^{13,17}$-structure.[22] Oxidation of the diol (LXVe) gave

the diketone (LXVc), confirming the epimeric nature of com-

pounds (LXVd) and (LXVa) and the structure of the ether

(LIIId).

The reaction mixture from the β-epoxide (XLVh) was

separated by preparative t.l.c. to give the "backbone" compound

(LVIIIc) (16%), the ketone (LVc) (5%) and the aldehyde

(LIIa) (34%). A further fraction (14.5%) was an inseparable

mixture.

The backbone-rearranged compound (LVIIIc) was identified

from its [1]H n.m.r. and mass spectral data. The former shows

the lower half of the $C(21)H_3$— doublet at τ 9.00 and the

14β-methyl signal at τ 9.06. Double irradiation 88 Hz.

downfield from the $C(21)H_3$-doublet causes its collapse.[2]

The mass spectrum of the compound (LVIIIc) has intense peaks

(m/e 345, 285) and a base peak (m/e 267), corresponding to

loss of side chain, side chain plus acetic acid and side chain

plus acetic acid and water respectively. This supports the

$\triangle^{13,17}$ - structure.[22] Hydrolysis of the acetate

(LVIIIc) followed by oxidation gave the diketone (LVIIIb)

previously obtained from compound (LVIIIa) and so confirmed

the structure (LVIIIc).

The ketone (LVc) shows a carbonyl band at 1720 cm.[-1]

in the i.r. spectrum. The [1]H n.m.r. spectrum confirms the

assigned 5α-stereochemistry, the C(3)-methine proton being

axial (W$\frac{1}{2}$., ca. 18 Hz.).

The aldehyde (LIIa) was converted into the γ-lactone

(LXI). Both compounds were identical to those obtained

previously.

The reaction of the β-epoxide (XLVi) with boron trifluoride

repeatedly gave a complex mixture, from which no identifiable

products were isolated.

The reaction mixture from the 3α-acetoxy-5,6α-epoxide

(XLVd) was separated by preparative t.l.c. to give the

Westphalen derivative (LVIIe) (43%), the backbone-rearranged

compound (LVIIId) (21%), the ketone (LVd) (28%) and the

aldehyde (LIIb) (2.8%).

The Westphalen derivative (LVIIe) was identified from its

[1]H n.m.r. and u.v. spectra and by hydrolysis and oxidation

to give the diketone (LVIIb) which was previously obtained

from compound (LVIIa). The backbone-rearranged compound

(LVIIId) was identified from its [1]H n.m.r. and mass spectra

and by conversion into the diketone (LVIIIb) which was

previously obtained from compound (LVIIIa). The ketone (LVd)

shows a carbonyl band ($\nu_{max.}$ 1710 cm.$^{-1}$) and the axial

3β-methine proton (W$\frac{1}{2}$., ca. 24 Hz.) is apparent from the

[1]H n.m.r. spectrum.

The aldehyde group in compound (LIIb) is apparent

from the i.r. (2700, 1720 cm.$^{-1}$) and [1]H n.m.r. (τ0.27)

spectra. In the latter spectrum the 3β-methine proton is

axial ($W\frac{1}{2}$., ca. 24 Hz.) indicating the 5β-stereochemistry.

The aldehyde (LIIb) was oxidised with Jones reagent[20] and

hydrolysed to give the crude hydroxy-acid (LXc). Treatment

of the hydroxy-acid (LXc) with toluene-p-sulphonic acid in

benzene gave the lactone (LXI) (14.5%),which was previously

obtained from the aldehyde (LIIa). The formation of the

lactone (LXI) from compound (LIIb) occurs by an alkyl-oxygen

cleavage mechanism. Such a mechanism is not as favourable

as the normal acyl-oxygen cleavage mechanism[71] and this could

account for the low yield of the lactone (LXI) from compound

(LIIb).

Reaction of the 5α,6α-epoxide (XLVf) gave a mixture

which was separated by preparative t.l.c. to give four

fractions which were then acetylated. Further t.l.c. of

the first and third fractions gave the Westphalen derivative

(LVIIf) (10.5%) and the ether (LIIIe) (17%). Preparative t.l.c.

of the second fraction gave the ketone (LVd) (10.5%) and a

mixture. Hydrolysis and subsequent oxidation of this mixture

followed by preparative t.l.c. gave the diketone (LIXb) (5%).

Hydrolysis and subsequent oxidation of the fourth fraction,

followed by preparative t.l.c. gave the ether (LXX) (4.3%).

The Westphalen derivative (LVIIf) was identified from

the [1]H n.m.r. and u.v. spectra and by its conversion into

the diketone (LVIIb). The ether (LIIIe) was identified by

its conversion into the keto-ether (LIIIc) which was

previously obtained from compound (LIIIb). The [1]H n.m.r.

spectrum of the ether (LIIIe) shows that the 6β-methine proton

is deshielded ($\triangle$ 0.17 ppm) by the 3α-acetoxy group relative

to the 6β-methine signal for the ether (LIIIa). A similar

deshielding of the 6β-methine proton was observed for the

two compounds (LXVd) and (LXVa) ($\triangle$ 0.25 ppm). This lends

further support to the assigned 3α-stereochemistry for the

compound (LXVd).

The ether (LXX) has been assigned a tentative structure

on the following evidence. The i.r. spectrum shows a cyclo-

hexanone carbonyl band (1720 cm.$^{-1}$) and no hydroxyl bands.

The ^{1}H n.m.r. spectrum shows a single,3β-methine proton

(τ 5.75, W$\frac{1}{2}$., ca. 13 Hz.) and the 13β-methyl at τ 9.28.

These data are consistent with those reported by Hartshorn

et al.[32] for the compound (LXXI). Treatment of the

ether (LXX) with boron trifluoride in benzene for 30 minutes[32]

gave a single crude product which was oxidised to give the

$\triangle^9$-diketone (LVIIb). The above data do not allow the

alternative structures for the ether [(LXXII) and (LXXIII)] to

be completely excluded.

The 5β,6β-epoxide (XLVe) was treated with boron trifluoride

for 12 hr. The reaction mixture was acetylated and separated

by preparative t.l.c. to give the ketone (LVe) (67%) and the

triacetate (LXXIV) (12.5%). The i.r. spectrum of the

ketone (LVe) shows a carbonyl band (1720 cm.$^{-1}$) and the

^{1}H n.m.r. spectrum shows the 3β-methine proton to be equatorial

(W$\frac{1}{2}$., ca. 8 Hz.). The structure of the triacetate (LXXIV)

follows from the ^{1}H n.m.r. spectrum which shows equatorial

methine protons at C(3) (W$\frac{1}{2}$., 10 Hz.) and C(6)(W$\frac{1}{2}$.,ca.5Hz.)

and three acetoxy groups. The mass spectrum of compound

(LXXIV) shows no molecular ion or [M-HOAc] ion. The first

fragment ion observed (m/e 440) is due to loss of 2 moles of

acetic acid from the molecular ion.

The reaction of the 5β,6β-epoxide (XLVg) with boron

trifluoride produced a complex mixture which has not been

effectively purified.

In contrast to the 5α,6α-epoxide (XIVd),[1b,2] the epoxide

(XLVb) gives a low yield (17%) of the corresponding fluoro-

hydrin. It is possible that the increased bulkiness of

the angular ethyl group in compound (XLVb) increases the

hindrance to axial approach of the fluoride ion at C(6) and

so allows other reaction paths to compete. This would also

explain the absence of fluorohydrins in the products from

the 3α-substituted-5,6α-epoxides (XLVd) and (XLVf) whereas

the epoxides (XIVf)[38] and (XIVg)[32] give measurable

quantities (8% and 47% respectively) of the fluorohydrins.

The failure of the 5β,6β-epoxide (XLVh) to give any

of the fluorohydrin (LXXVI), and the low yield of the

5α-acetate (LXXIV), formed via the acetonium ion (LXXV),[32]

from the 5β,6β-epoxide (XLVe), may also be due to the bulky

angular ethyl group which would prevent formation of an

axial 6β-hydroxyl group. Compare the reactions of the

epoxides (XIVe)[1b] and (XIVh).[32]

The formation of the 5β-aldehyde (LIIa) from the

epoxide (XLVb) must involve a discrete C(5) carbonium ion.

LXXVII

LXXVIII

LXXIX

LXXX

(a) 5,6α
(b) 5,6β

LXXXI

LXXXII

LXXXIII
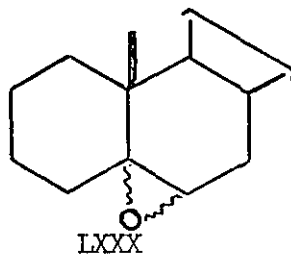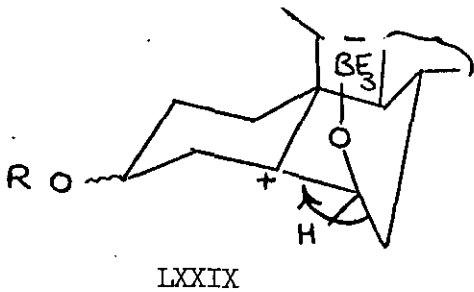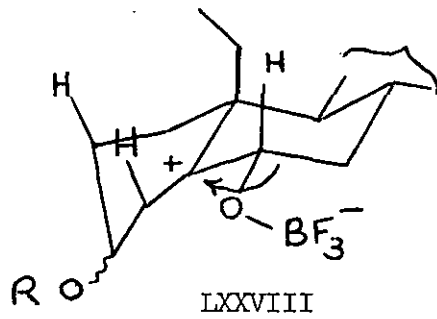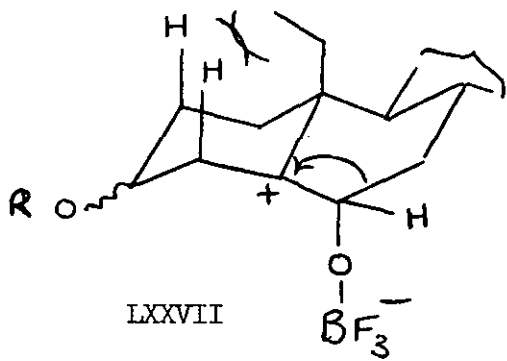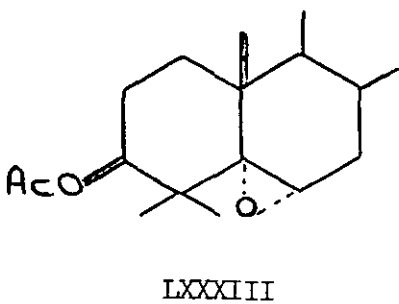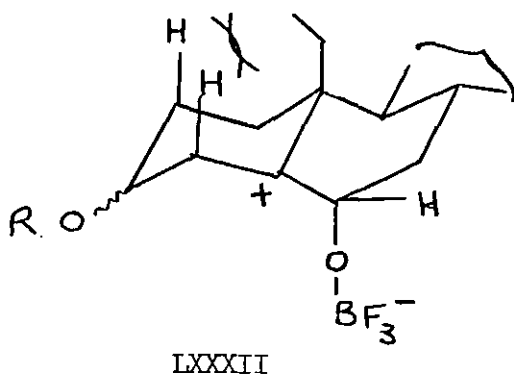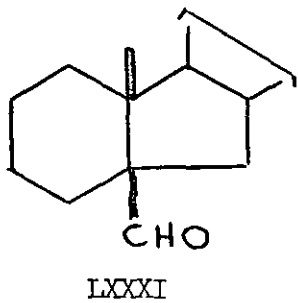
The originally formed carbonium ion (LXXVII) would give

the 5α-aldehyde (LXII) on migration of the C(6)-C(7) bond.

The aldehyde (LIIa) may be formed from a C(5) carbonium ion

in the conformation (LXXVIII). This conformation would

afford some relief of the steric interactions between the

10β-ethyl-group and the syn-2- and-4-hydrogen atoms. The

formation of the aldehyde (LIIb) from the epoxide (XLVd)

would occur in a similar manner. The formation of the aldehyde

(LIIa) from the β-epoxide (XLVh) could occur directly from the

initially formed C(5) carbonium ion (LXXIX). It is reported

that the epoxides (LXXXa,b) give rise to the same aldehyde

(LXXXI); the mechanism proposed is the same as above.[24]

The formation of the spiro-compounds (LIII, LIX) from

the epoxides (XLVa,b,c,f) also requires a fully developed

C(5) carbonium ion since cis-migration of the C(1)-C(10)

bond is necessary. The increased yields of the spiro-

compounds from the 10β-ethyl-epoxides (XLVa,b,c,f) in

contrast to their 10β-methyl analogues (XIVa,d,c,g) may

also be explained by the increased 10β-alkyl interactions

with the syn-2-and-4-hydrogen atoms in the former epoxides.

This could cause a flattening of the A-ring in the carbonium

ions (LXXVII) or (LXXXII), so pushing the C(1) atom towards

the C(5) atom. This flattening would be opposed by developing

non-bonding interactions between the C(3)-substituent and

C(2) and C(4) methylene protons as they start to eclipse.

Similar arguments have been used to account for the formation

of the spiran (XI) from the epoxide (Xa).[6] In the case of

the epoxide (LXXXIII), the potential non-bonding interactions

between the 3β-acetoxy- and 4β-methyl-group is so great as

to prevent the A-ring flattening and no spiro-compound is

formed from this epoxide.[6]

The formation of the "backbone compound" (LVIIIa) from the

epoxide (XLVb) in low yield (3%) is also unusual. Possibly

the migration of a hydride ion from C(8) to C(9) is more

hindered in the 5β-ethyl compounds than in their 5β-methyl

analogues. An alternative possibility is that the ethyl

group involves torsional and angular conformational strain

in the A,B ring system which is sufficient to limit the

rearrangement to the relief of this local strain rather than

that of the remote C,D ring system.[56]   Using either

argument, replacement of the 3β-acetoxy-group by a

3α-acetoxy-group would reduce the 3β-substituent, 5β-ethyl

group, 1,3-non-bonding interaction and therefore give a

greater yield of the backbone-rearranged compound. This

was observed, although the yield of the compound (LVIIId)

(21%) is still not as great as that of the 10β-methyl-

-analogue (XVIIIg) (37%) from the compound (XIVf).[38]

The formation, in high yields, of the backbone compounds

(LXV) from the spiro-ethers (LIII) is in agreement with the

above arguments.

In terms of the competition between C(5)-O cleavage

and fluorohydrin formation the effect of changing the

3β-substituent follows the same general trend as was observed

previously (see Discussions 1 and 2).   Some of this work

has recently been reported by us in the literature.[72]

42.

Discussion 4:-

Homoallylic participation of the 5,6-double bond in
the solvolyses of 3- and 19-sulphonyloxy-steroids is
believed to give intermediate non-classical carbonium ions
from which the various products are derived.[73]   The
boron trifluoride catalysed rearrangements of the 10β-
-ethenyl-steroids (LXXXIVa,b,c) provides a system where
participation of the homoallylic ethenyl group could occur
to give intermediate, stabilised non-classical carbonium ions.
The availability of these epoxides (LXXXIVa,b,c) prompted
the investigation of their reactions with boron trifluoride.

The hydroxy-epoxide (LXXXIVa) was the sole product from
the monoperphthalic acid oxidation of the diene (XLVII).
The structure was confirmed by the ^{1}H n.m.r. spectrum of
compound (LXXXIVa) and by acetylation to give the known
acetoxy-epoxide (LXXXIVb).[74]

Reaction of the hydroxy-diene (XLVII) with trimethyl-
orthoformate and perchloric acid[62]   gave the methoxy-diene
(LXXXV).[60]   Monoperphthalic acid oxidation of compound
(LXXXV) gave the 5,6α-epoxide (LXXXIVc). The ^{1}H n.m.r.
spectrum of the epoxide (LXXXIVc) shows a single epoxide
proton (τ 7.13 J. (apparent) 4 Hz.), supporting the assigned
structure.[49]

The reaction mixture from the boron trifluoride treatment
of the acetoxy-epoxide (LXXXIVb) was separated by preparative
t.l.c. to give the backbone-rearranged dimer (LXXXVI) (26%)
and the fluorohydrin (LXXXVIIa) (47%). Some epoxide

43.

LXXXIV

$$
\begin{array}{ll}
& \text{R} \\
\text{(a)} & \text{H} \\
\text{(b)} & \text{Ac} \\
\text{(c)} & \text{Me}
\end{array}
$$
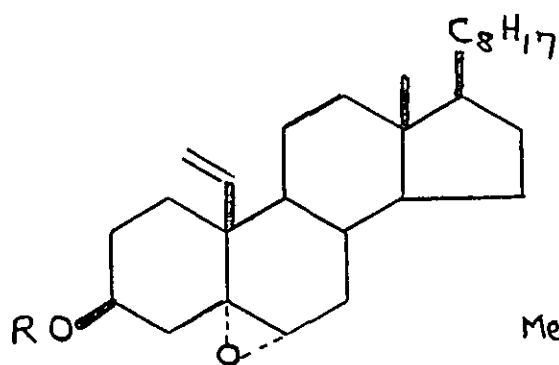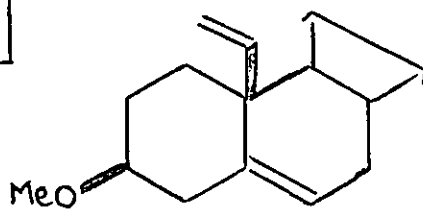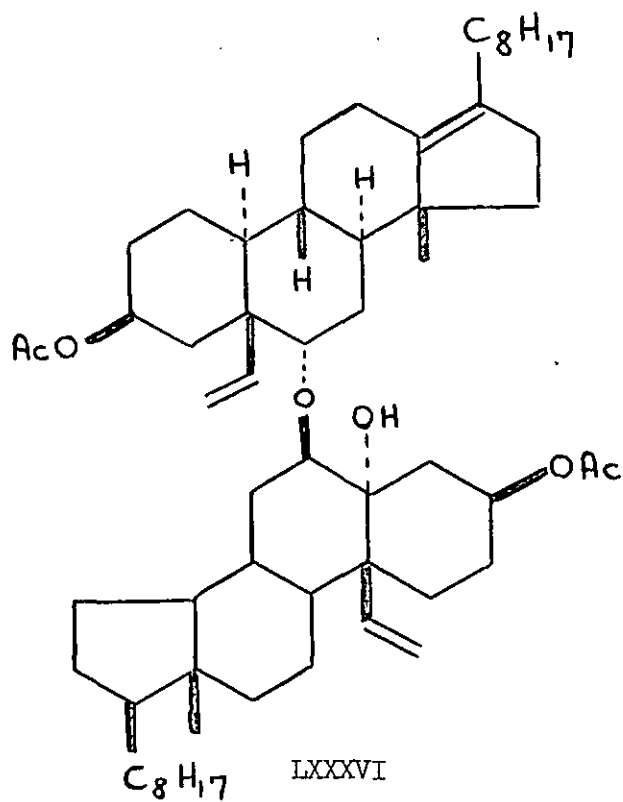
LXXXV

LXXXVI

(LXXXIVb) (18%) was recovered from the reaction mixture; the quoted yields allow for this.

, The dimer (LXXXVI) was identified from its 100 M.Hz. ^{1}H n.m.r. spectrum in which the C(21)H$_3$-doublet (τ 9.06, J. 7 Hz.) collapsed to a singlet (τ 9.06) on double irradiation at 144 Hz. downfield.[2] Other important multiplets appear at τ 2.8-4.2 (α-vinyl-2H), τ 4.5-5.4 (β-vinyl-4H, C(3)-2H), and τ 6.66 and τ 6.76 (C(6)-2H). The 13β-methyl group appears at τ 9.46 for the 'normal' half of the dimer. The dimeric nature of the compound (LXXXVI) was confirmed by a molecular weight determination (osmometry 882; the dimer requires 912).

The fluorohydrin (LXXXVIIa) was readily identified from its ^{1}H n.m.r. spectrum which shows the 6α-methine proton (τ 5.7, doublet of multiplets, J_{HF}, ca. 50 Hz.) and the 5α-hydroxyl proton (τ 6.6, singlet exchanged with D$_2$O). Treatment of the fluorohydrin (LXXXVIIa) with methanolic potassium hydroxide gave the epoxide (LXXXIVa), supporting the assigned structure.

The reaction mixture obtained from the hydroxy-epoxide (LXXXIVa) was inseparable. Acetylation followed by preparative t.l.c. gave only one identifiable product, the fluorohydrin (LXXXVIB) (33%).

Preparative t.l.c. of the reaction mixture from the methoxy-epoxide (LXXXIVc) gave the fluorohydrin (LXXXVIIb) (16%), the backbone-rearranged-product (LXXXVIII) (2%)
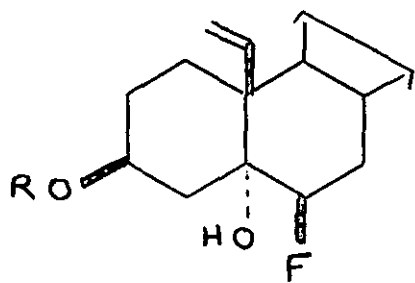
LXXXVII
R
(a) Ac
(b) Me
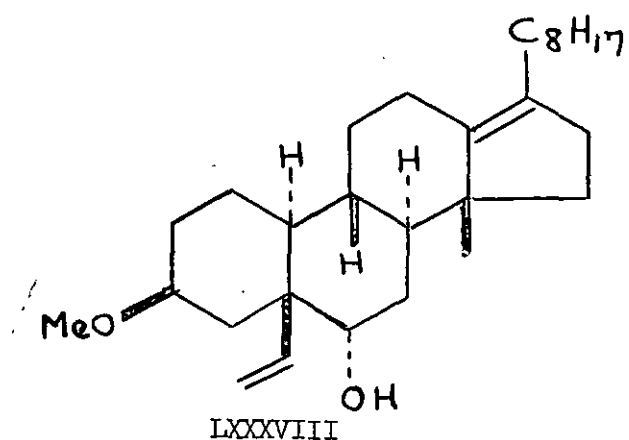
LXXXVIII
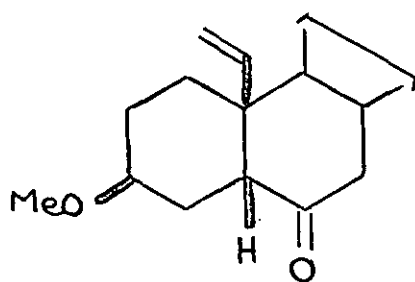
LXXXIX
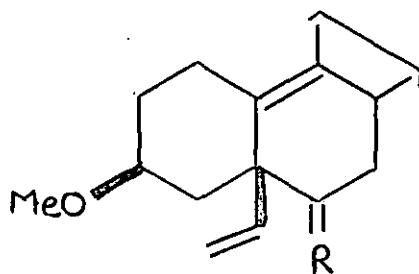
XC
R
(a) αOAc,H
(b) =O
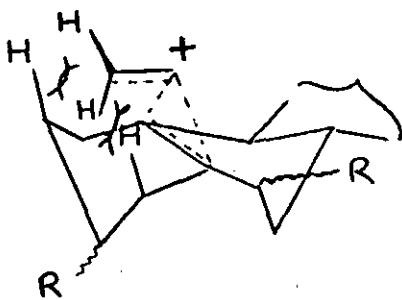
XCI
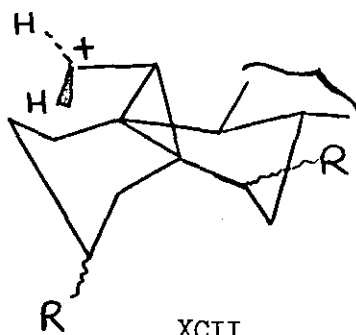
XCII

and the ketone (LXXXIX) (15%). Acetylation of another fraction

followed by t.l.c. gave the Westphalen derivative (XCa) (13%).

The remaining material (37%) could not be separated. The

quoted yields allow for the recovery of some of the epoxide

(LXXXIVc) (6%).

The fluorohydrin (LXXXVIIb) was identified from its

^{1}H n.m.r. and i.r. spectra. The former shows the 6α-

methine proton as a doublet of multiplets (τ 5.60, J_{HF} ca.

50 Hz.), and the latter shows the presence of the tertiary

hydroxy-group (3630, 3450 cm.$^{-1}$). The backbone-rearranged

compound (LXXXVIII) was identified from its ^{1}H n.m.r. spectrum

which shows the C(21)H$_3$-doublet (τ9.06, J. ca. 6 Hz.) and

the 14β-methyl group (τ 9.19). Double irradiation 88 Hz.

downfield caused the collapse of the C(21)H$_3$-doublet.[2]

The mass spectrum of the compound (LXXXVIII) shows a base

peak (m/e 297) due to the characteristic loss of side chain[22]

and water from the molecular ion. The i.r. spectrum of the

ketone (LXXXIX) shows a carbonyl band (1713 cm.$^{-1}$). The

^{1}H n.m.r. spectrum of the ketone (LXXXIX) shows an equatorial

C(3)-methine proton (W½. 7 Hz.) and confirms the 5β-stereo-

chemistry. The ^{1}H n.m.r. spectrum of the Westphalen derivative

(XCa) shows a typical 13β-methyl signal (τ9.21).[12] The

u.v. spectrum indicates a non-conjugated diene. Hydrolysis

and oxidation of the compound (XCa) gave the ketone (XCb).

The structure is supported by the ^{1}H n.m.r. spectrum of

the ketone (XCb) which shows the 13β-methyl group at τ 9.22

and by the i.r. spectrum which shows a carbonyl band at

1718 cm.$^{-1}$.

The attempted hydrogenation of the ketone (XCb) to give the

ketone (LVIId), using a palladium — charcoal catalyst gave

a mixture which was not investigated any further.

The epoxide (LXXXIVb) reacts in a similar manner to

3β-acetoxy-5,6α-epoxy-5α-cholestane (XIVd).[1b,2] Thus

surprisingly the C(19)-methylene group appears to have little

effect on the product distribution. The participation of

the olefinic bond does not appear to compete very favourably

with attack of fluoride ions at C(6). Although this is not

direct evidence regarding the ionic intermediates from the

epoxide (LXXXIVb) it does seem unlikely that non-classical

ions of the type (XCI)[75] are particularly favourable energetically.[31]

Steric interaction between one of the methylene hydrogen atoms

and the hydrogen atoms at C(2) and C(4) may be a factor in

destabilising ions of the type (XCI).[75] This would not

apply to the classical ion (XCII) or the equivalent non-

-classical bicyclobutonium ion.[75,76]

Overlap of the π electrons of the olefinic bond with the

developing (or fully developed) C(5) carbonium ion could lead

to the classical ions (XCII) and (XCIII), and thus the ion

(XCIV). The product (LXXXVI) could then be derived from the

ions (XCII) and (XCIV). The above arguments will apply

equally as well to the 3β-hydroxy- and 3β-methoxy-epoxides

(LXXXIVa,c).

The epoxides (LXXXIVa,c) give increased yields of their

respective fluorohydrins (LXXXVIIa,c) in a comparison with

the analogous 10β-methyl epoxides (XIVa,c). This would
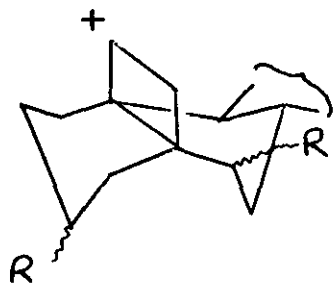
XCIII
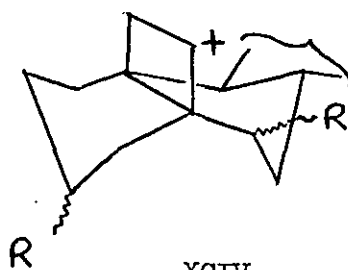
XCIV
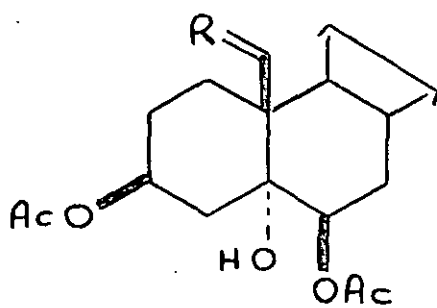
XCV

	R
(a)	CH_2
(b)	H_2

indicate that the ethenyl group is inductively destabilising

C(5)-oxygen cleavage. This could occur in a stepwise or a

concerted process. In the latter, the destabilisation would

be analogous to that reported for phenyl migration.[77]

The yield of the fluorohydrin (LXXXVIIa) (47%) from

epoxide (LXXXIVb) in comparison to that of the fluorohydrin

(XVb) (ca.70%) from the epoxide (XIVd)[1b] is an apparent

contradiction to the above argument. This prompted a

re-investigation of the reaction of the epoxide (XIVd)

with boron trifluoride, under the same conditions used for

the epoxide (LXXXIVb).

The yield of the fluorohydrin (XVb) was 43% and thus the

comments on the inductive (-I) effect of the 10β-ethenyl group

seem reasonable.

The same general conclusions have been reached in a

recent study of the Westphalen rearrangement of the 10β-ethenyl-

-compound (XCVa).[60a,78] It was found that the product

distribution resembled that from the rearrangement of the

10β-methyl compound (XCVb), although the reaction rate was

slower for the former compound. The observed scrambling of

a deuterium label in the ethenyl group also supported these

conclusions.[60a,78]

The ethenyl group would be expected to be sterically

less demanding than the ethyl group. The yield of the

backbone-product (LXXXVI) (26%) from the 10β-ethenyl-epoxide

(LXXXIVb) in comparison to that of the compound (LVIIIa) (3%)

from the 10β-ethyl-epoxide (XLVb) may be due to this.

Backbone-rearranged compounds are normally isolated as monomers. The reason for the isolation of the backbone compounds (IX) and (LXXXVI) as dimers is not clear.

SECTION 2

The Lewis acid catalysed reactions

of some 9,10-epoxy-19-nor-cholestanes

and epoxy-lanostanes.

Introduction:-

In contrast to trisubstituted epoxides, tetrasubstituted epoxides have no overwhelming electronic preference for cleavage of a particular C-O bond when treated with a Lewis acid. From a conformational analytical study of the reactions of a number of 4,5- and 5,6-tetrasubstituted steroidal epoxides Kirk and Hartshorn[79] formulated the rule of axial cleavage. This states that any 1,2-disubstituted epoxy-cyclohexane will tend to react by cleavage of the C-O bond which permits the oxygen atom to become axial in the chair conformation of the ring most nearly corresponding to the half chair conformation of the original epoxide. The rationale of this rule was that axial cleavage could lead to a continued partial overlap of the filled orbital of the departing oxygen atom with the formally vacant p-orbital of the carbonium ion, thus minimising the energy of the transition state prior to bond migration. This continued orbital overlap would also have a directing effect on which migrations could occur, leading to a preference for trans-migration. Equatorial cleavage would give none of these effects.

It has been found that 'axial cleavage' can be overcome by the operation of adverse conformational, steric, or electronic effects. Thus it was found that the rearrangements of the four epimeric 3-acetoxy-4,5-epoxy-4-methyl-cholestanes (XCVI) exhibited 'abnormal' reactions,[80] i.e. equatorial cleavage. Where normal axial cleavage is permitted then

XCVI

XCVII

XCVIII

XCIX

C

CI
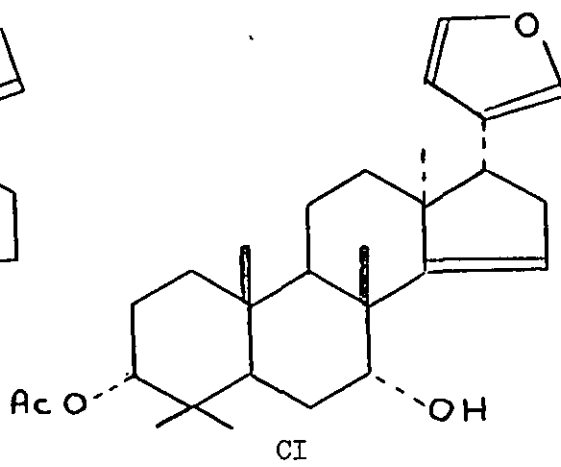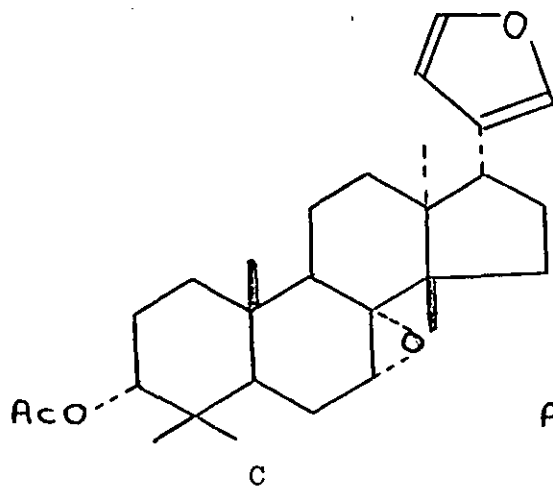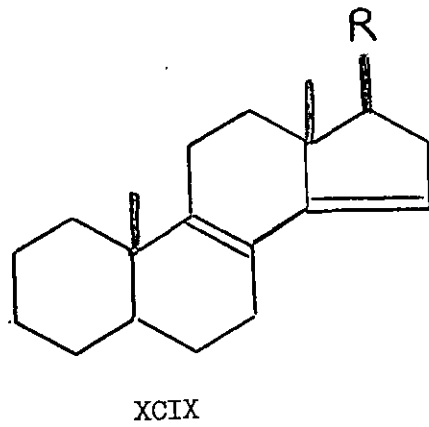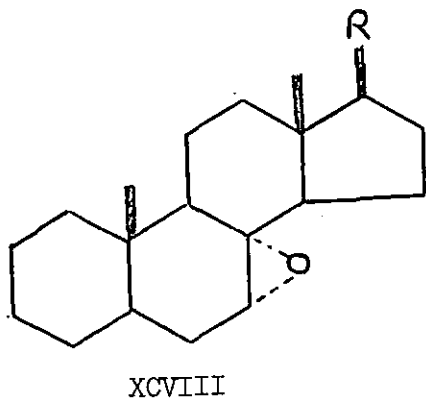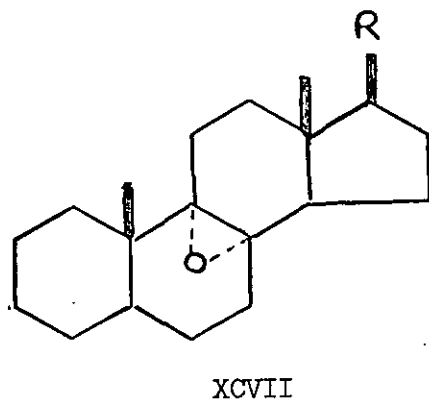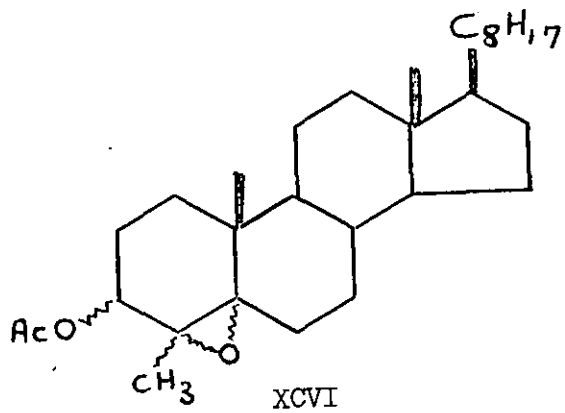
bond migrations which result in charge accumulation at C(4) are suppressed by the 3-acetoxyl-group.

The lack of ketone formation from epoxides of the type (XCVII) and (XCVIII) has been noted.[1a,81,82] Both these epoxides give the diene (XCIX). The failure to give carbonyl compounds has been attributed to conformational restraints opposing deformation and bond migration in the centre of the steroid nucleus and to the thermodynamic stability of the conjugated diene system.[1a] Halsall[83] has found that the 7,8α-epoxide (C) gives the hydroxy-olefin (CI).

The boron trifluoride catalysed reactions of some C(6)-substituted-9,10-epoxy-5β-methyl-19-nor-cholestanes (CII) have been studied to further examine the effects of possible conformational restraints in the centre of the steroid nucleus, and to provide further information on the "backbone-rearrangement" of steroidal epoxides. In contrast to the 7α,8α- and 8α,9α-epoxides (XCVII and XCVIII) a number of 9,11-epoxides have been found to give a wide range of interesting products.

Henbest[1a] investigated the boron trifluoride catalysed reactions of the two epoxides (CIIIa) and (CIIIb) and found that the epoxide (CIIIb) rearranged quickly to give the expected, strain free ketone (CIVa) whereas the epoxide (CIIIa) rearranged slowly to give the strained ketone (CIVb). Wechter[84] treated the epoxide (CV) with boron trifluoride

CII

CIII

(a) 9α,11α
(b) 9β,11β

CIV

(a) 9α
(b) 9β
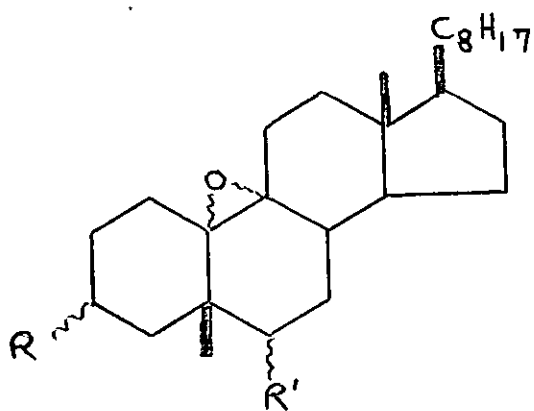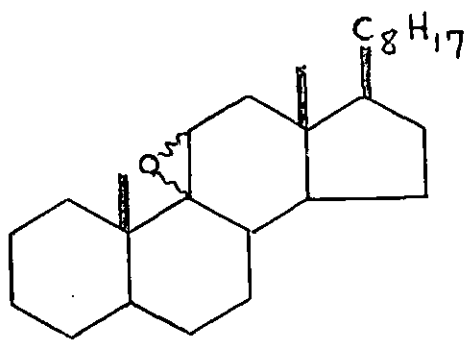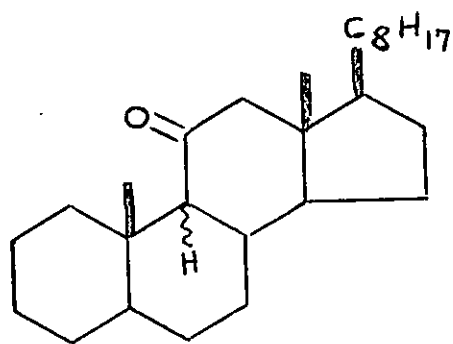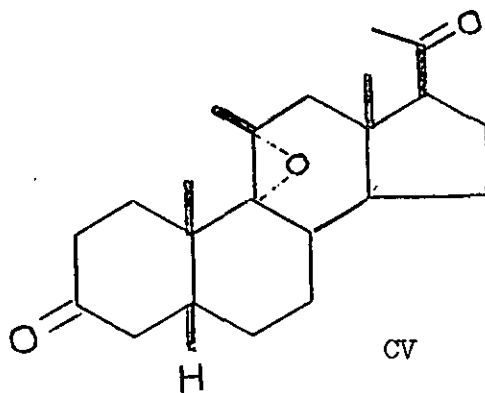
CV
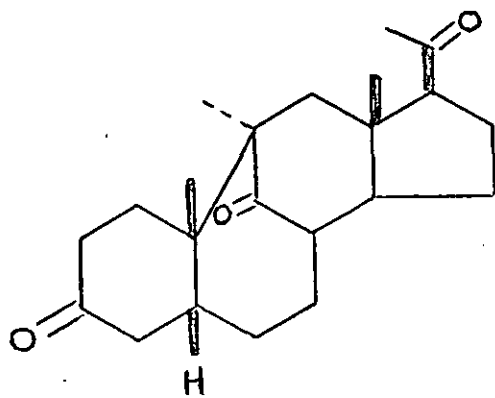
CVI
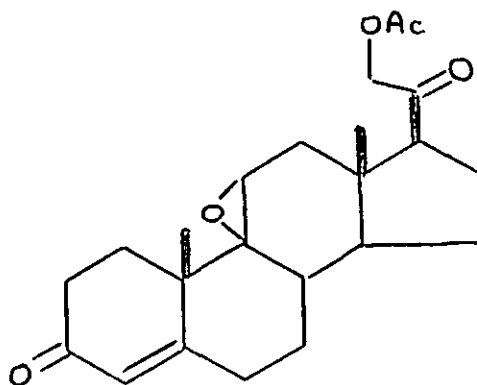
CVII

and obtained the ketone (CVI) in high yield, and this is

consistent with the rule of axial cleavage. Treatment of the

epoxide (CVII) with perchloric acid gave as the major

product (CVIII) and only a small yield of the 11-ketone[85]

The 9α-hydrogen in the product (CVIII) arose from a 1,3-

-transannular shift of the 14α-hydrogen atom. No explanation

has been offered for the difference between this reaction

and the analogous one employing boron trifluoride.

The 9,11-epoxides provide potential precursors for

partial synthesis of the cucurbitacins, for example,

bryogenin (CIX). ApSimon et al.[86] found that the epoxides

(CIXa) and (CIXb) would not react with boron trifluoride

etherate and reacted only slowly with boron trifluoride gas.

The major products were the olefins (CXIa,b) and not as

expected the phenols (CXIIa,b). Formation of the homoallylic

alcohols was considered to occur by intramolecular removal

of the 14α-hydrogen atoms by the 9α-oxygen atoms, there being

no ether present to act as a proton transfer agent.

The 3β-acetoxy-8,9α-epoxy-and-9,11α-epoxy-lanostanes

were studied as potential intermediates in cucurbitacin

synthesis and in view of the diversity of the recorded reactions

of 9,11-epoxides[1a,84,85,86] the reactions of 3β-acetoxy-

-9,11α-epoxy-lanostane with Lewis acids would also be of

a more general interest.

CVIII

CIX

CX

R
(a) =0
(b) βCOCH₃,H

CXI

R
(a) =0
(b) βCOCH₃,H
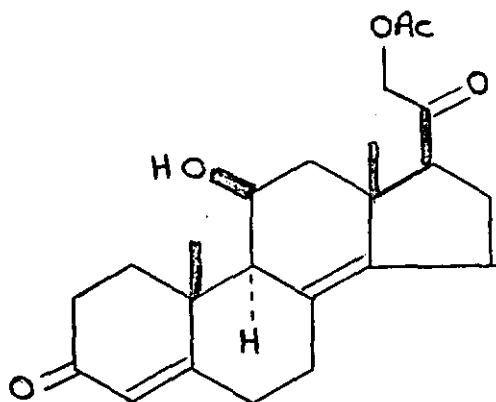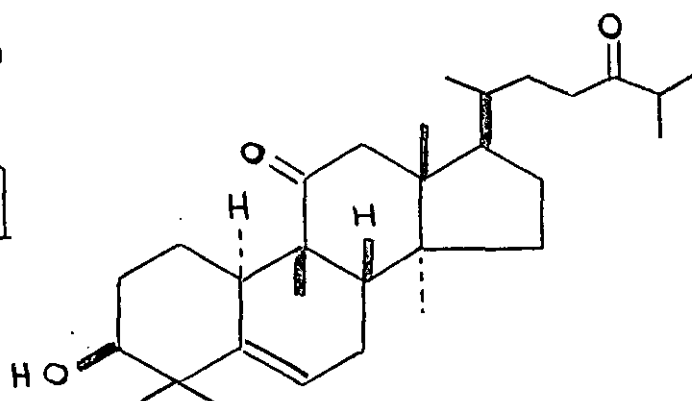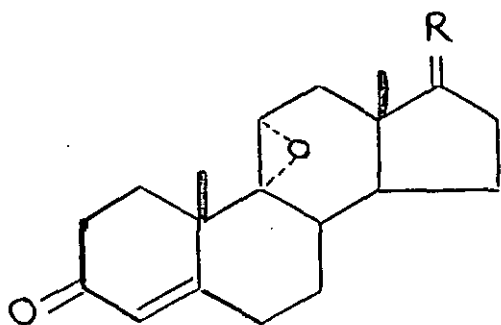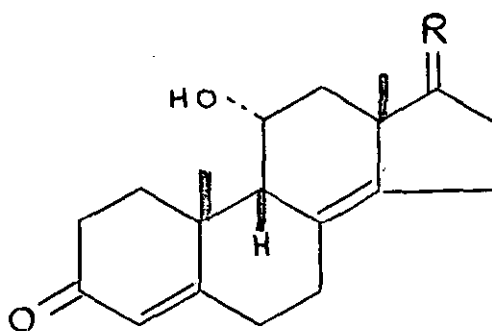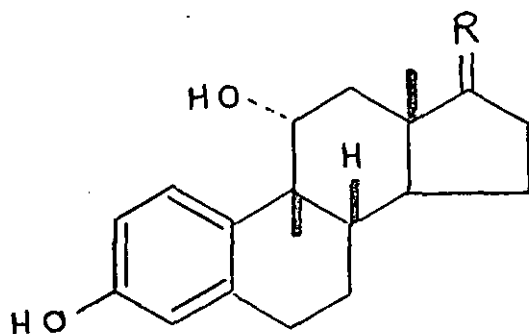
CXII

R
(a) =0
(b) βCOCH₃H

Discussion 1:-

The epoxide mixture (CXIIIa,b) was prepared via the

Westphalen compound (CXIVa) by the method of Mousseron-Canet.[87]

Repeated preparative t.l.c. of this mixture gave the pure

α-epoxide (CXIIIa) (51%) and β-epoxide (CXIIIb) (34%). The

5β-methyl signals in the [1]H n.m.r. spectra for the α-epoxide

(CXIIIa) (τ 8.78) and the β-epoxide (CXIIIb) (τ 8.84)

allowed the stereochemistry of the epoxides to be assigned,

by analogy with the observed relative chemical shifts of the

10β-methyl groups of some 5α,6α- and 5β,6β-epoxides.[49]

Hydrolysis of the 6β-acetoxy-α-epoxide (CXIIIa) gave the

6β-hydroxy-α-epoxide (CXIIIc). Oxidation of compound

(CXIIIc) with Jones reagent[20] in acetone gave the known

6-oxo-α-epoxide (CXIIId),[88] which had previously been

prepared by oxidation of the Westphalen derivative (CXIVb).

Similar treatment of the 6β-acetoxy-β-epoxide (CXIIIb) gave

the 6β-hydroxy-β-epoxide (CXIIIe) and the 6-oxo-β-epoxide

(CXIIIf).

The 6-desoxy-epoxides (CXIIIg,h) were prepared from the

6-desoxy-Westphalen compound (CXIVc). The compound (CXIVc)

had previously been prepared in 50% yield, by the Huang-Minlon

reduction of the 6-ketone (CXIVb).[28] In an attempt to

improve the yield of this step, the reduction of the benzene

sulphonyl hydrazone (CXIVd) was attempted. These reactions

are reported to proceed in high yield with other steroidal

ketones.[89] The benzene sulphonyl hydrazone (CXIVd) was

prepared from the ketone (CXIVb) according to Barton,[90]

and was found to be a relatively unstable compound.

CXIII

		R
(a)	9α,10α	βOAc,H
(b)	9β,10β	βOAc,H
(c)	9α,10α	βOH,H
(d)	9α,10α	=O
(e)	9β,10β	βOH,H
(f)	9β,10β	=O
(g)	9α,10α	=H$_2$
(h)	9β,10β	=H$_2$
(i)	9α,10α	β,p-CH$_3$PhSO$_3$,H
(j)	9α,10α	PhNHN=
		SO$_2$

CXIV

	R
(a)	βOAc,H
(b)	=O
(c)	H$_2$
(d)	PhNHN=
	SO$_2$

CXVI

	R
(a)	=O
(b)	βOAc,H

CXV

	R
(a)	=O
(b)	βOAc,H
(c)	=H$_2$

Sodium borohydride reduction of the freshly prepared compound

(CXIVd) in dioxan[89] gave the required 6-desoxy-compound

(CXIVc). The yield of the 6-desoxy-compound (CXIVc) was

found to be extremely variable. Acceptable yields (ca.

80%), were only obtained from small scale reactions and no

other identifiable products were isolated from the reactions.

The compound (CXIVc) was therefore prepared by the literature

method.[28] Oxidation of the compound (CXIVc) using mono-

perphthalic acid gave the mixed epoxides (CXIIIg,h).

Preparative t.l.c. of the mixture gave the pure α-epoxide

(CXIIIg) (48%)and pure β-epoxide (CXIIIh) (32%). The stereo-

chemistry of the epoxides (CXIIIg and h) was assigned from

^{1}H n.m.r. spectral evidence,[49] as described previously.

Several attempts to prepare the α-epoxide (CXIIIg) from

the epoxides (CXIIIc) and (CXIIId) have proved unsuccessful.

The tosylate (CXIIIi) and the benzene sulphonyl hydrazone

(CXIIIj) could not be formed.

Treatment of the 6-oxo-α-epoxide (CXIIId) with boron

trifluoride gave a mixture. Preparative t.l.c. of this mixture

gave the diene (CXVa)[88a](24%), the diene (CXVIa)[88a](24%),

the backbone-rearranged compound (CXVIIa) (20%), and the

backbone-rearranged compound (CXVIIIa) (6%). The dienes

(CXVa) and (CXVIa) were previously obtained by treatment of

the epoxide (CXIIId) with ethanolic hydrochloric acid.[88a]

The 100 M.Hz.^{1}H n.m.r. spectrum of the backbone-rearranged

compound (CXVIIa) shows a single vinylic proton (τ 4.66)

and characteristic signals for the 5β-methyl group (τ 8.64),

CXVII

R

(a) =O
(b) βOAc,H
(c) =H₂

$$R$$

CXVIII

R
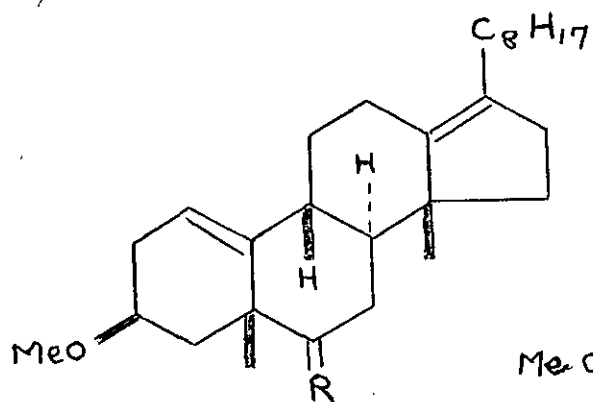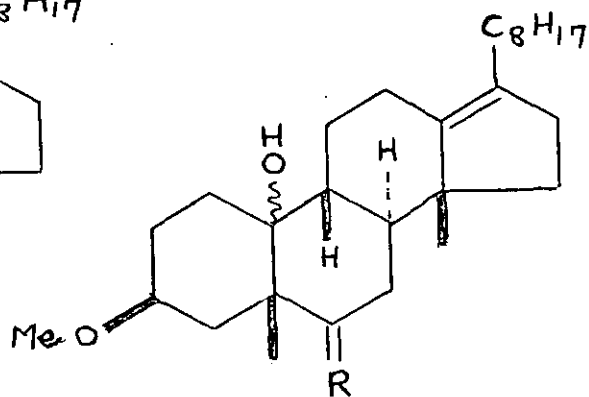
(a) 10α   =O
(b) 10β   =O
(c) 10β   βOAc,H

CXX
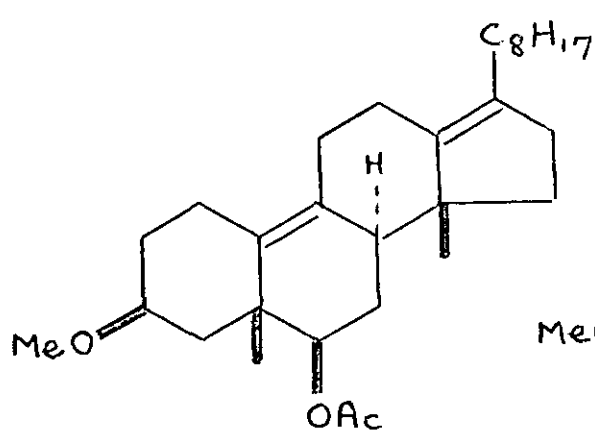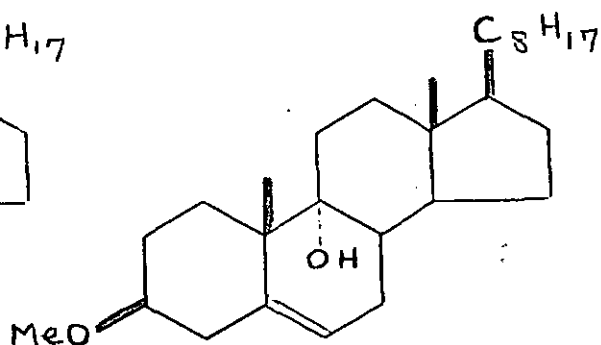
CXXI

the 14β-methyl group (τ 8.99), and the C(21)H$_3$-doublet

(τ 9.07 J. ca 7 Hz.). The 60 M.Hz. [1]H n.m.r. spectrum of

the compound (CXVIIa) in d$_6$-benzene shows upfield shifts for

the 5β-methyl group (τ 8.83) and 14β-methyl group (τ 9.15)

signals.[91] The lower branch of the C(21)H$_3$ doublet is

observed at τ 8.93. Double irradiation 88 Hz. downfield

caused the collapse of this doublet confirming the $\triangle^{13,17}$-

-structure.[2] The $\triangle^{1,10}$-structure is supported by the low

field position of the 5β-methyl group signal. The axial

C(3) methine proton (W$\frac{1}{2}$ ca. 22 Hz.) is also consistent with

a $\triangle^{1,10}$- or 5β,10β-structure. The mass spectrum of the

compound (CXVIIa) shows an intense peak (m/e 267) due to loss

of side chain and methanol from the molecular ion (m/e 412).

This supports the assigned $\triangle^{13,17}$-structure.[22] Hydrogenation

of the compound (CXVIIa) using a palladium-charcoal catalyst

gave a mixture of two isomeric compounds, inseparable by

t.l.c. . The [1]H n.m.r. spectrum of the mixture shows a

predominance (ca. 70%) of one isomer which appears to possess

the 10β-configuration since the C(3) methine proton is axial

(W$\frac{1}{2}$ ca. 22 Hz.). The observed upfield shift of the 5β-methyl

signals (τ ca. 8.73) on hydrogenation of compound (CXVIIa) is

consistent with the assigned structure. The 14β-methyl-

groups signals of the dihydro-compounds (τ ca. 9.00)were

unchanged on hydrogenation, as would be expected. This

mixture was not further investigated.

The structure of the compound (CXVIIIa) is tentatively

assigned on the following evidence. The i.r. spectrum indicates

the presence of a hydroxyl group (3620, 3500 cm.$^{-1}$). The ^{1}H

n.m.r. spectrum shows the 5β-methyl group (τ 8.61) and the

14β-methyl group (τ 9.00). The equatorial C(3)-methine proton

(W½ ca. 9 Hz.) is consistent with the 5β,10α-stereochemistry.

In d$_6$-benzene an upfield shift of the 5β-methyl group (τ 9.05)

and 14β-methyl group (τ 9.14) signals is observed[91,92] to

reveal half of the C(21)H$_3$ doublet (τ 8.93)   at low field.

This would be expected for a $\triangle^{13,17}$-structure. The

decomposition of the compound (CXVIIIa) prevented further data

from being obtained.

Reaction of the β-epoxide (CXIIIf) with boron trifluoride

gave a mixture. Preparative t.l.c. of the mixture gave the

diene (CXVa) (23%), the diene (CXVIa) (26%), the backbone-

rearranged compound (CXVIIa) (5%), the backbone-rearranged

compound (CXVIIIb) (7%), and the diketone (CXIXa) (5%).

The i.r. spectrum of the compound (CXVIIIb) shows a

hydroxyl band (3500 cm.$^{-1}$). The ^{1}H n.m.r. spectrum of the

compound shows the 5β-methyl group (τ 8.81), the 14β-methyl

group (τ 9.02), and the lower half of the C(21)H$_3$-doublet

(τ 9.00). The axial C(3)-methine proton (W½ ca. 22 Hz.)

supports the assigned 10β-stereochemistry. The spectrum in

d$_6$-benzene shows the 5β-methyl and 14β-methyl signals shifted

upfield and the lower half of the C(21)H$_3$ doublet clearly

resolved. Double irradiation 88 Hz. downfield caused the collapse

of this doublet and confirmed the $\triangle^{13,17}$-structure.[2]

Treatment of the compound (CXVIIIb) with thionyl chloride

C₈H₁₇ structures labeled A, B, C, D

MeO ... A

MeO ... B

MeO ... C

MeO ... D

R

(a) =O

(b) =H₂
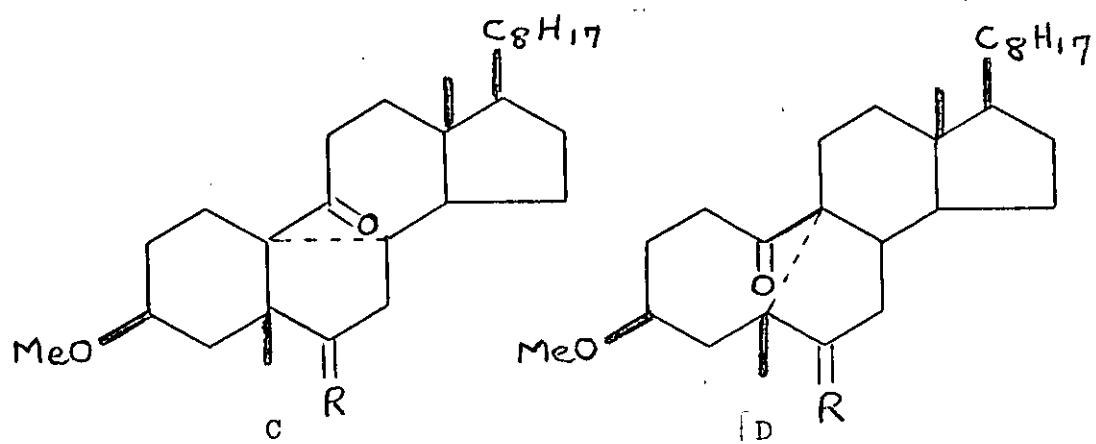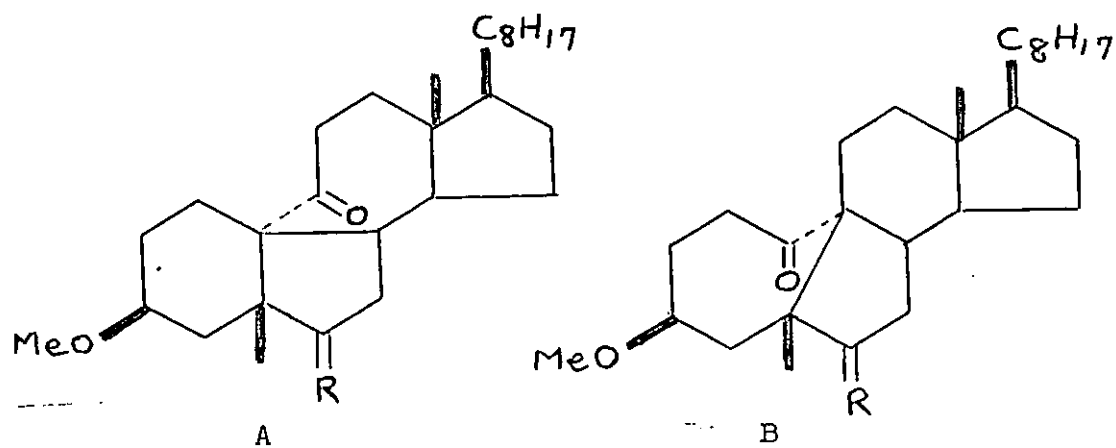
CXIX

in pyridine gave the diene (CXVIIa), identical with an authentic sample (by t.l.c.).

The i.r. spectrum of the diketone (CXIXa) shows cyclopentanone (1730 cm.$^{-1}$) and cycloheptanone (1700 cm.$^{-1}$) carbonyl bands, The ^{1}H n.m.r. spectrum of the diketone shows the 5β-methyl group (τ 8.79) and the 13β-methyl group (τ 9.33). The C(3)-methine proton signal is obscured by the 3β-methoxyl signal and its half-height band width could not be determined. As the conformations of the cycloheptanone rings in any of the structures (CXIXa) are not known it is difficult to determine the shielding or deshielding effect of the cycloheptanone carbonyl group on the angular methyl group signals. Therefore a definite structure cannot be assigned. The structures (CXIXAa) and (CXIXBa) would both involve the migration of a group which is _cis_ to the departing oxygen atom in the epoxide (CXIIIf). This would involve a high degree of carbonium ion character at either C(9) or C(10), and this would be expected to be unfavourable owing to the presence of the inductive (-I) effect of the C(6)-oxo-group. The structures (CXIX Ca) and (CXIX Da) both involve migrations of groups _trans_ to the departing oxygen-atom and so the rearrangement could retain some degree of concerted character and this might be expected to be more favourable under the prevailing conditions.

Treatment of the α-epoxide (CXIIIa) with boron trifluoride gave a mixture. Preparative t.l.c.

gave the backbone-rearranged compound (CXVIIb) (56%), and the

backbone-rearranged compound (CXX) (3%).

The ^{1}H n.m.r. spectrum of the compound (CXVIIb) shows

a single vinylic proton (τ 4.68), the 5β-methyl group

(τ 8.88), the 14β-methyl group (τ 9.03) and the lower

branch of the C(21)H$_3$-doublet (τ 9.00). Double irradiation

87 Hz. downfield from the C(21)H$_3$-doublet caused its collapse,

verifying the $\Delta^{13,17}$-structure.[2] The mass spectrum of

the compound (CXVIIb) shows an intense peak (m/e 343) due

to loss of side chain from the molecular ion (m/e 456). This

is consistent with the assigned $\Delta^{13,17}$-structure.[22]

Hydrolysis and oxidation of the 6β-acetoxy-compound (CXVIIb)

gave the 6-oxo-compound (CXVIIa), identical with an authentic

sample (by t.l.c. and ^{1}H n.m.r.).

The i.r. spectrum of the compound (CXX) shows no hydroxyl

band. The ^{1}H n.m.r. spectrum shows the 5β-methyl group

(τ 8.82), the 14β-methyl group (τ 9.07) and the lower half

of the C(21)H$_3$-doublet (τ 9.00). Double irradiation

87 Hz. downfield from the latter signal collapsed this doublet,

confirming the $\Delta^{13,17}$-structure.[2] The similarity in

the chemical shift of the 5β-methyl group and that of the

5β-methyl group in the compound (CXIVc) (τ 8.85) and the

equatorial C(3)-methine proton (W$\frac{1}{2}$ ca. 10 Hz.) are consistent

with a $\Delta^{9,10}$-structure.

A further minor hydroxylic-product (5%) was isolated.

This compound, from which the 3β-methoxyl-group had been

removed, decomposed before sufficient data was available for

its identification.

The reaction mixture from the β-epoxide (CXIIIb) was separated by preparative t.l.c. to give the conjugated diene (CXVb) (34%), the conjugated diene (CXVIb) (17%), and the backbone-rearranged compound (CXVIIIc) (15%). The u.v. spectra of the diene (CXVb) ($\lambda_{max.}$ 249 n.m., $\epsilon_{max.}$ 25,200) and the diene (CXVIb) ($\lambda_{max.}$ 243 n.m., $\epsilon_{max.}$ 9,200) compare well with those reported for the compounds (CXVa) and (CXVIa).[88a] The ^{1}H n.m.r. spectra of (CXVb) and (CXVIb) also compare well with those of compounds (CXVa) and (CXVIa).

The i.r. spectrum of the compound (CXVIIIc) shows the presence of a hydroxyl group (3620, 3450 cm^{-1}).The ^{1}H n.m.r. spectrum shows the 5β-methyl group (τ 9.00), the 14β-methyl group (τ 9.09), the $C(21)H_3$-doublet (superimposed on the 5β-methyl signal , and lower branch of the side chain doublet τ9.12). Double irradiation 90 Hz. downfield from the $C(21)H_3$-doublet caused a reduction in the intensity of the signals at τ9.00 and 9.12 and an increase in the intensity of the signal at τ 9.09. The structure of compound (CXVIIIc) was confirmed by its conversion to compound (CXVIIb) with thionyl chloride in pyridine.

Reaction of the α-epoxide (CXIIIg) with boron trifluoride gave a complex mixture. Preparative t.l.c. of the mixture gave the backbone-rearranged compound (CXVIIc) (27%), the ketone (CXIXb) (28%), the hydroxy-olefin (CXXI) (9%) and a further diene (CXXII) (18%).

CXXIII

CXXIV

CXXV

CXXVI
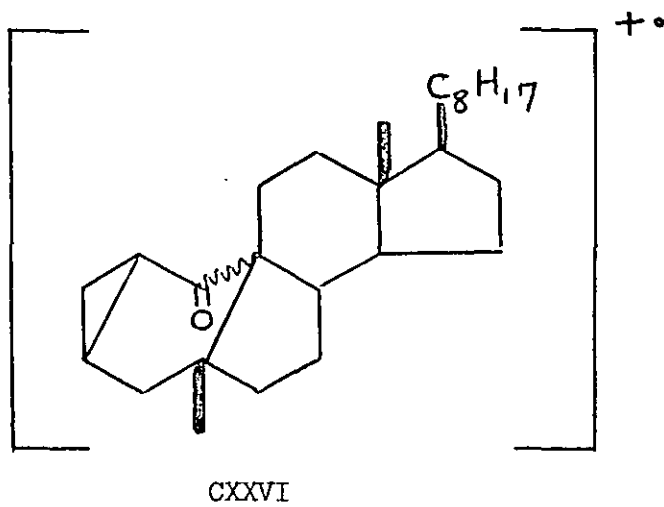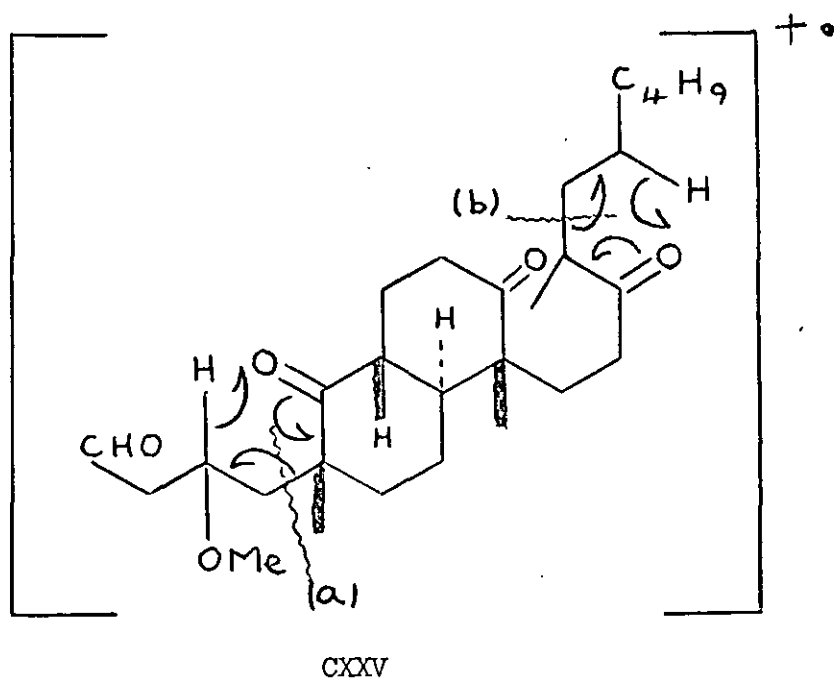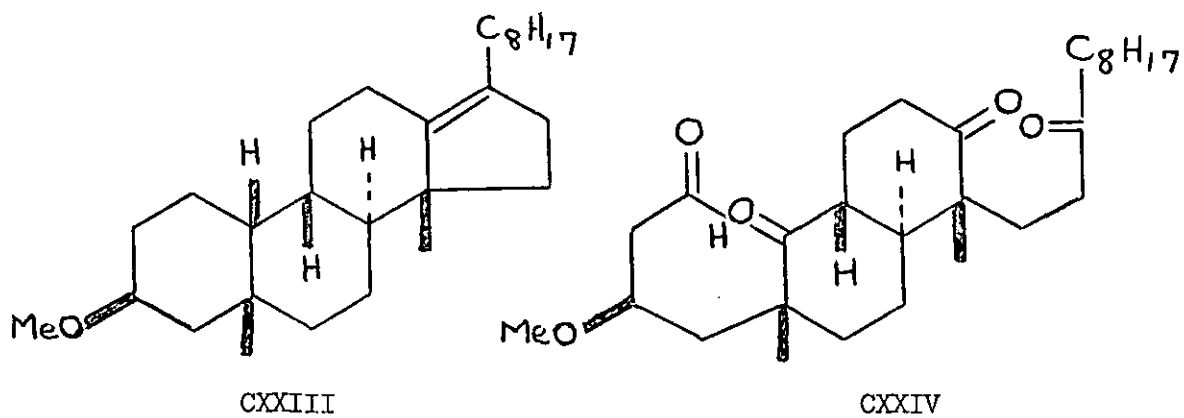
The ^{1}H n.m.r. of the diene (CXVIIc) was typical of a $\triangle^{1(10),13(17)}$-structure, as described previously. Double irradiation experiments and the mass spectrum confirmed the $\triangle^{13,17}$-structure.[2,22] Hydrogenation of the diene (CXVIIc) using a palladium-charcoal catalyst gave a single compound (CXXIII). The 10β-stereochemistry was indicated by an axial C(3) methine proton (τ 6.65-7.20) in the ^{1}H n.m.r. spectrum. The 5β-methyl group signal (τ 9.00) was shifted upfield relative to that for compound (CXVIIc) (τ 8.91). This shift (-0.09 p.p.m.) is similar to that observed on hydrogenation of the compound (CXVIIa). The compound (CXXIII) was not further investigated. Ozonolysis of the diene (CXVIIc) gave a mixture. Preparative t.l.c. gave the pure tetrone (CXXIV) (23%). The ^{1}H n.m.r. spectrum (τ 0.23, triplet, J. ca. 2.5 Hz.) and i.r. spectrum (2720 cm.$^{-1}$) of the compound (CXXIV) confirmed the presence of the -CHO group. The ^{1}H n.m.r. spectrum also showed the C(21)H$_3$-doublet at low field (τ 8.93, J. ca 7 Hz.). The mass spectrum shows an intense peak (m/e 362) due to loss of the A-ring carbon atoms from the molecular ion (m/e 462) by a McLafferty rearrangement (CXXV, fission (a)).[64] A strong peak (m/e 378) corresponding to the loss of side chain from the molecular ion by a similar mechanism is also observed (CXXV fission (b)). These fragmentations are consistent with the assigned structure.

The i.r. spectrum of the ketone (CXIXb) shows a carbonyl band (1705 cm.$^{-1}$). The ^{1}H n.m.r. spectrum shows

the 5β- and 13β-methyl signals superimposed (τ 9.05). The

mass spectrum of the compound (CXIXb) shows an intense peak

(m/e 384) due to loss of methanol from the molecular ion

(m/e 416). This fragmentation is not observed in the mass

spectrum of the ketone (CXIXa). This, and comparison of

the [1]H n.m.r. data for the two ketones (CXIXa) and (CXIXb)

suggests they have a different carbon skeleton. The loss

of methanol in the mass spectrometer is normally a 1,3-

or 1,4-elimination.[93,a,b] The enhanced loss of methanol

in the mass spectrum of the ketone (CXIXb) (m/e 384, 37%),

was thought to be possibly due to the formation of an ion

(CXXVI) of enhanced stability. Preliminary deuteration

experiments have however proved inconclusive. Schaffner

et.al.[94] have recently reported the formation of some

8(9 → 10)abeo-10α-and 10β-steroidal ketones by the photolysis

of some 9α,10α- and 9β-10β-epoxides.

The compound (CXXI) shows a hydroxyl band (3590 cm.$^{-1}$)

in its i.r. spectrum. The hydroxyl group was found to be

resistant to acetylation using acetic anhydride/pyridine,

and to oxidation using Jones reagent.[20] The [1]H n.m.r.

spectrum of the compound (CXXI) shows a single vinylic proton

(τ 4.66), two angular methyl groups (τ 8.88, 9.42) and

an axial C(3)-methine proton (τ 6.4-6.8). Dehydration of

the compound (CXXI) with thionyl chloride in pyridine gave

a single product, the diene (CXXVII). The u.v. spectrum

indicates a non-conjugated diene. This eliminates the

possibility of a $\triangle^{1,10}$- partial structure. The [1]H n.m.r.

CXXVII

CXXVIII

CXXXII

R

(a) =O
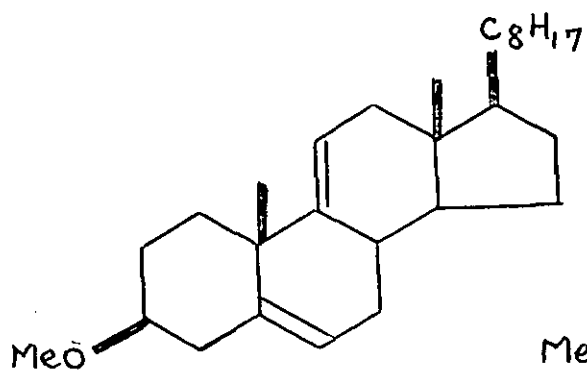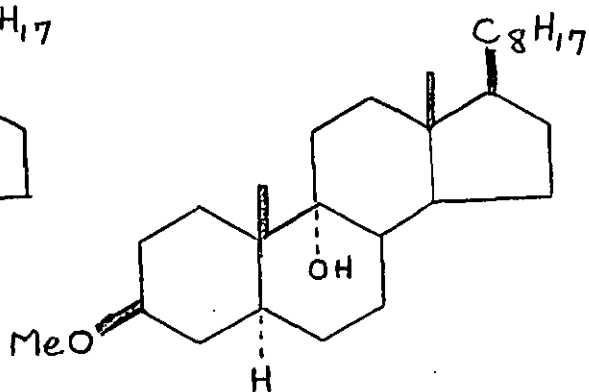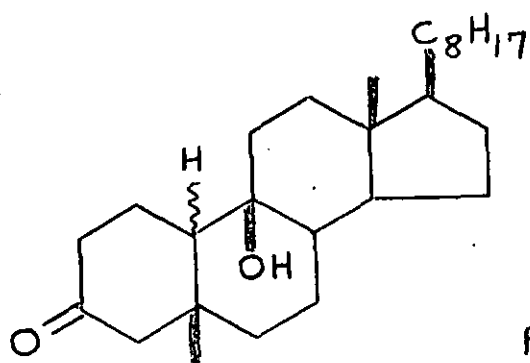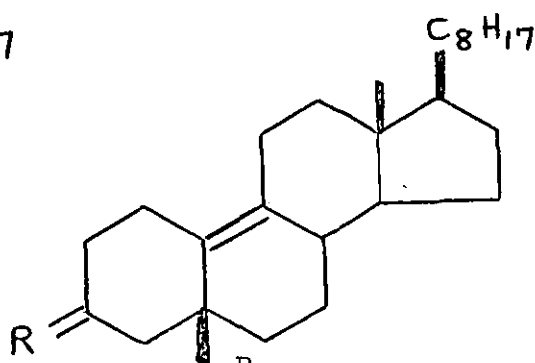
(b) βOH,H

CXXXIII
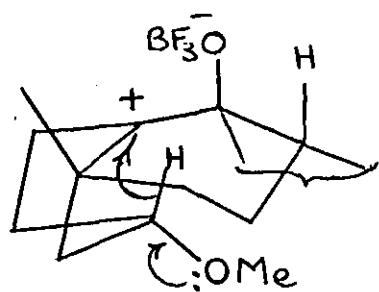
CXXXIV
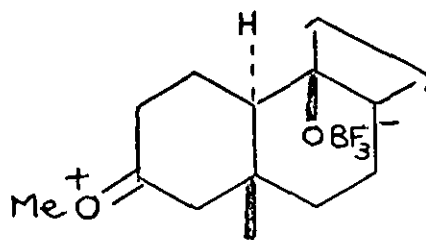
CXXXV

spectrum shows the angular methyl groups (τ 8.75, 9.37)

and two vinylic protons. The calculated positions for

the 10β-methyl and 13β-methyl groups[46] of the compounds

(CXXI) and (CXXVII) were found to be in reasonable agreement

with the experimental values (table 1).   A $\triangle^{5,6}$-

-structure as opposed to a $\triangle^{4,5}$-structure was assigned

on the basis of the half-height band width of the vinylic-

proton (W$\frac{1}{2}$ 10 Hz.) for the compound (CXXI).   Hydrogenation

of the hydroxy-olefin (CXXI) using a platinum catalyst in

acetic acid gave two compounds, separated by preparative

t.l.c.. The major product (53%) was identified as 3β-methoxy-

cholestane,[33] by comparison with an authentic sample.

This confirms the structure of the compound (CXXI).   The

minor product (10%) has been assigned the structure (CXXVIII)

from its [1]H n.m.r. (see table 1) and i.r. spectral data.

Compound	Observed 10β-methyl signal	Calculated[46] 10β-methyl signal	Observed 13β-methyl signal	Calculated 13β-methyl signal
CXXI	8.88	8.83	9.42	9.31
CXXVII	8.75	8.83	9.37	9.38
CXXVIII	9.02	9.06	9.32	9.35

TABLE 1

The structure of the remaining diene (CXXII) (see

fig.1) rests on the following evidence. The i.r. spectrum

of the compound (CXXII) shows no hydroxyl or carbonyl bands.

The mass spectrum of the compound shows the molecular ion

(m/e 398) as the base peak and a peak (m/e 285, 22%) due

to the loss of side chain. These data could be consistent

with a diene structure (molecular formula $C_{28}H_{46}O$) with

one of the olefinic bonds in the centre of the molecule

but not at C(13)-C(17).[29]   The u.v. spectrum of the

compound indicates a non-conjugated diene system. The

^{1}H n.m.r. spectrum shows a single vinylic proton (τ 4.75),

an axial C(3)-methine proton ($W\frac{1}{2}$ ca. 24 Hz), and the angular

methyl groups (τ 9.13, 9.20).   The C(21)H_3-doublet was not

observed at low field, indicating that a 13,17-olefinic bond

was absent. The chemical shifts of the angular methyl signals

indicated that the 13β-methyl group was highly deshielded

and therefore an 8,14- or 14,15-olefinic bond could be

present.   A $\triangle^{14,15}$- partial structure would require a

tetrasubstituted 9,10-olefinic bond.   This is not consistent

with the observed axial C(3)-methine proton, or the relatively

high field positions of the angular methyl signals [c.f.

compound (CXIVc); 5β-methyl (τ 8.85)].   A $\triangle^{1(10),8(14)}$-diene

system would also require a 5β-methyl group signal at low

field as the 5β-methyl group would be deshielded by both

olefinic bonds.   An examination of a molecular model of the

compound (CXXII) indicates that the C(6)-vinylic proton

would couple to only one of the C-(7) protons.   This would

be consistent with the observed narrow multiplet ($W\frac{1}{2}$ ca. 6 Hz.)
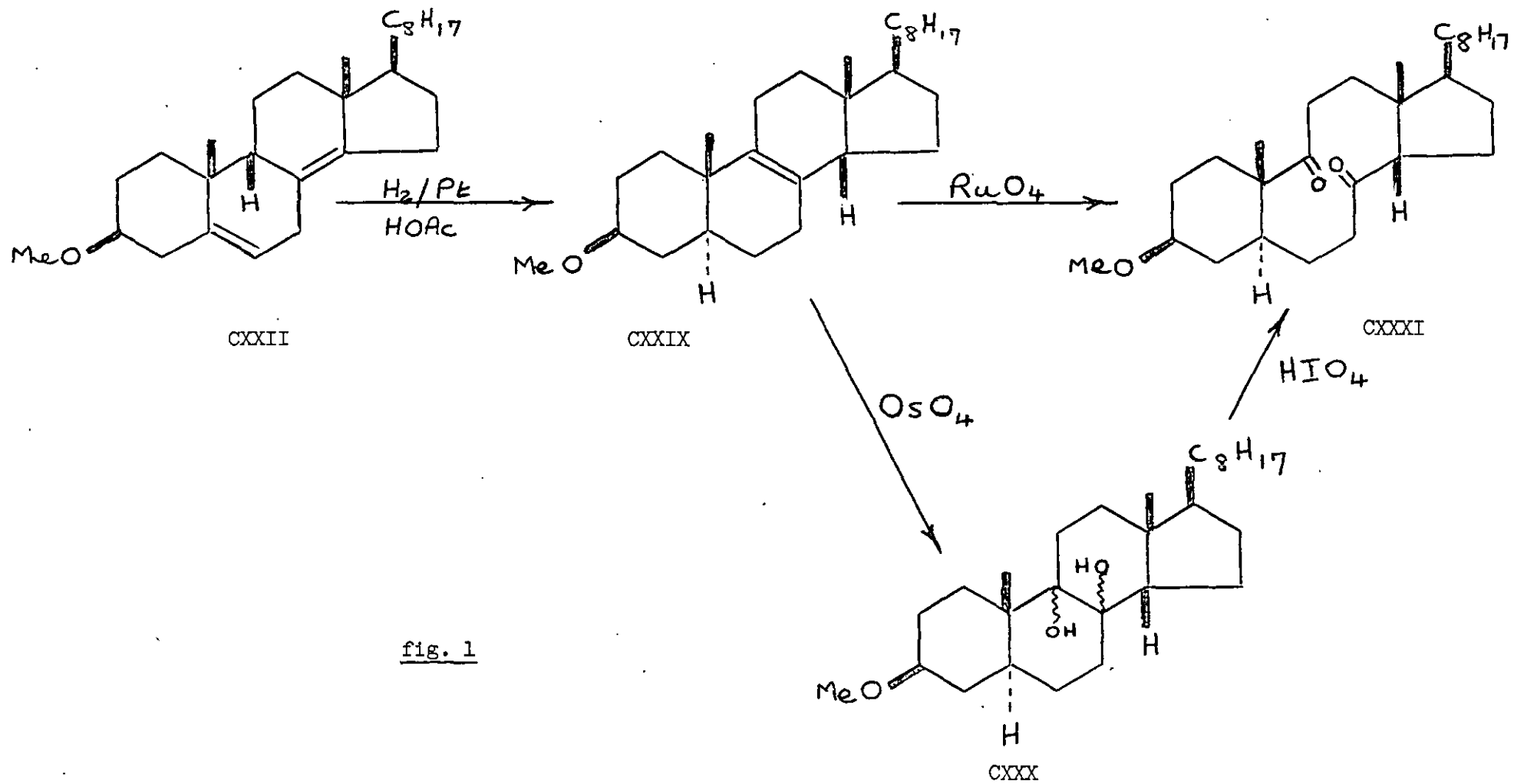
fig. 1

for the vinylic proton signal. Hydrogenation of the diene using

a platinum catalyst in acetic acid gave the olefin (CXXIX).

The mass spectrum of the compound (CXXIX) shows the molecular

ion (m/e 400) as base peak and a peak (m/e 287, 13%) due to loss

of the side chain. The ^{1}H n.m.r. spectrum of the compound

(CXXIX) shows an axial C(3)-methine- proton (τ 6.55-7.15) and

the angular methyl group signals (τ 9.13, 9.37). The

angular methyl group signals in the ^{1}H n.m.r. spectra of both

compounds (CXXII) and (CXXIX) were identified by the addition

of the paramagnetic shift reagent, tris-dipivalomethanato-

europium [Eu (DPM)$_3$].[95]   A standard steroid: Eu(DPM)$_3$

molar ratio, and a standard concentration were employed.

The results are summarised in table 2. The compound (CXVIIc)

and 3β-methoxycholest-5-ene were used as reference compounds.

The results enable the 13β-methyl group signals to be

assigned unambiguously for the compounds (CXXII·) and (CXXIX)

but do not allow an unambiguous definition of the second

angular methyl group as 5β- or 10β-. However, the observed

COMPOUND	VINYLIC PROTON		METHOXYL METHYL		5β-METHYL		10β-METHYL		13β-METHYL	
	τ	Shift ppm	τ	Shift ppm	τ	Shift ppm	τ	Shift ppm	τ	Shift ppm
3β-methoxy-cholest-5-ene	4.73	0.18	6.76	1.53			9.00	0.17	9.33	0.03
CXVIIc	4.93	0.22	6.79	0.90	8.91	0.11			9.04	0.04
CXXII	4.75	0.08	6.79	1.49			9.13	0.13	9.20	0.02
CXXIX			6.80	1.30			9.13	0.13	9.37	0.04

TABLE 2

shift for the vinylic proton in compound (CXXII) (table 2) is more in keeping with a $\triangle^{5,6}$- than a $\triangle^{1,10}$-structure. These results thus support the proposed $\triangle^{5,8(14)}$-structure for compound (CXXII) and the $\triangle^{8(9)}$-structure for the compound (CXXIX). Isumerisation of the 8,14-olefinic bond to the 8,9-position presumably occurs on the catalyst surface during hydrogenation. If this is so then compound (CXXIX) would be expected to have the 14β-configuration,[96,97] since the diene (CXXII), from mechanistic considerations, has the 9β-configuration.

The compound (CXXIX) was found not to be 3β-methoxy-cholest-8-ene by comparison with the literature.[88a] However the chemical shift of the 13β-methyl group (τ 9.37) in the ^{1}H n.m.r. spectrum of the olefin (CXXIX) would seem to be far too high for a 14β-steroid.[46]

Treatment of the olefin (CXXIX) with ruthenium tetroxide[98] gave the dione (CXXXI). The same dione(CXXXI) was obtained from the olefin (CXXIX) by treatment with osmium tetroxide,[97,99] followed by periodic acid cleavage of the intermediate diol (CXXX). The dione (CXXXI) shows a single carbonyl band (1705 cm.$^{-1}$) in its i.r. spectrum, and this is consistent with the opening of an 8,9-olefinic bond.[97] The olefin (CXXIX) was treated with hydrogen chloride in chloroform to give a crude product. This was hydrogenated overnight using a platinum catalyst in acetic acid. The crude product, a mixture of olefinic and fully saturated material (by mass spectrometry) did not contain any 3β-methoxycholestane, as shown by t.l.c..

The structure of the diene (CXXII) and the reaction scheme (CXXII) $\longrightarrow$ (CXXXI) (fig.1) at present represent only a 'best fit' to the available data, although some of these data are not fully consistent with the reaction scheme. Until a degradation of the diene (CXXII) is achieved which allows the positive identification of the position of at least one of the olefinic bonds, a definite structure cannot be assigned to the diene. Preliminary experiments using osmium tetroxide or ruthenium tetroxide on the diene (CXXII) have provided no identifiable products.. Ozonolysis of the diene (CXXII) has given similar results.

Reaction of the β-epoxide (CXIIIh) with boron trifluoride gave a mixture. Preparative t.lc. of this mixture gave the backbone-rearranged compound (CXVIIc) (30%), the diene (CXXII) (8%), the conjugated diene (CXVc) (13%) and the ketone (CXXXII) (21%).

The conjugated diene (CXVc) was readily identified from its characteristic u.v. spectrum ($\lambda_{max.}$ 248 n.m., $\varepsilon_{max.}$ 27,000).[88a] The [1]H n.m.r. spectrum also supported the assigned structure.

The i.r. spectrum of the ketone (CXXXII) shows a carbonyl group (1720 cm.$^{-1}$) and hydroxyl group (3640, 3480 cm.$^{-1}$). The [1]H n.m.r. spectrum shows the 5β-methyl group (τ 9.09) and 13β-methyl group (τ 9.30) and no methine protons. The tertiary nature of the hydroxyl group was confirmed by its failure to acetylate using acetic anhydride in pyridine.

Exhaustive deuteriation of the ketone (CXXXII) using sodium

methoxide in deuterio-methanol indicates four exchangeable

protons are present (by mass spectrometry). Dehydration of

the hydroxy-ketone (CXXXII) with thionyl chloride in pyridine

gave a tetra-substituted olefin (CXXXIIIa). The i.r. spectrum

shows the carbonyl band (1715 cm.$^{-1}$). The ^{1}H n.m.r. spectrum

shows both the 5β-methyl (τ 9.00) and 13β-methyl (τ 9.20)

groups shifted downfield relative to those for compound (CXXXII).

Reduction of the compound (CXXXIIIa) with tri-(t-butoxy)-lithium

aluminium hydride[100] gave a single product, the hydroxy –

olefin (CXXXIIIb). The i.r. spectrum of compound (CXXXIIIb)

shows a hydroxyl group (3580, 3400 cm.$^{-1}$). The ^{1}H n.m.r.

spectrum also shows the 5β-methyl group (τ 8.75) and 13β-methyl

group (τ 9.21). The equatorial C(3)-methine proton (τ 5.90,

$W\frac{1}{2}$. ca. 9 Hz.) is consistent with the formation of the

3β-hydroxyl group. Treatment of the hydroxy-olefin (CXXXIIIb)

with potassium in refluxing benzene, followed by methyl iodide[33]

gave 3β-methoxy-5β-methyl-19-nor-cholest-9(10)-ene (CXIVc),

identical in all respects with an authentic sample.[28]

This verifies the structure of the keto-olefin (CXXXII).

The formation of the keto-olefin (CXXXII) could occur by

a 1,4-hydride migration from C(3) to C(10) as shown (CXXXIV)

to give the intermediate methoxonium ion (CXXXV).. Although

well documented in medium-sized ring compounds,[101]

transannular 1,4-hydride migrations are not well known in

cyclohexane ring systems. However a 1,4-phenyl shift has

been reported for a six-membered ring system.[102] A

66.
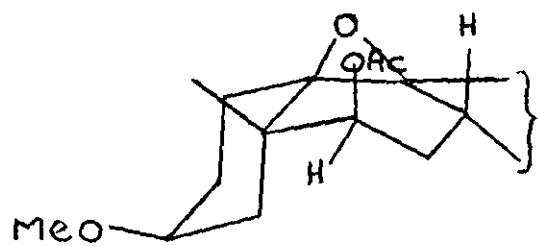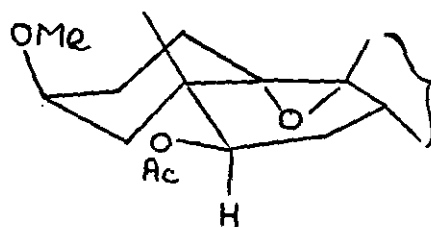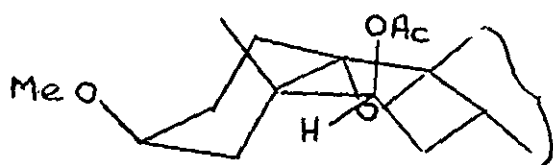
CXXXVI

CXXXVII

CXXXVIII

consequence of the mechanism proposed above is the 10α-
-stereochemistry for the compound (CXXXII). This is consistent
with the observed ready dehydration of the 9β-hydroxy-ketone
(CXXXII) to give the 9,10-olefin (CXXXIIIa). The above
mechanism could readily be proved by deuteriation experiments.
The alternative mechanism of a series of 1,2-hydride shifts
from C(1) and C(2) would involve the generation of secondary
carbonium ions and is therefore less likely.

The ^{1}H n.m.r. spectrum of the β-epoxide (CXIIIb) shows
an axial C(6)-methine proton as a quartet (J (apparent)
12 Hz., 4 Hz.). This indicates a conformation (CXXXVI) for
the epoxide. The ^{1}H n.m.r. spectrum of the α-epoxide
(CXIIIa) shows the C(6)-methine proton signal as a triplet
(J (apparent) ca. 10 Hz.). This could indicate a conformation
(CXXXVII) or alternatively a conformation (CXXXVIII) in which
the 7α- and 7β-protons exhibit accidental magnetic equivalence.[23]
The former conformation might be anticipated to be the more
stable of the two, since the 6β-acetoxy-group is equatorial.
In the cases of the 6-keto-epoxides (CXIIId,f) and
6-desoxy-epoxides (CXIIIg,h) the preference for any given half
chair conformation is not known. These conformational
ambiguities preclude the use of the axial cleavage rule[79]
for the 9,10-epoxides studied.

From the yields of backbone-rearranged products
obtained in the reactions described, it is clear that the
nature of the C(6)-substituent is a controlling factor on

the efficiency of the backbone-rearrangement. The inductive

(-I) effect of the C(6)-substituent would be expected to

affect the stability of any C(8) carbonium ion and so

affect the migratory aptitude of the 8β-hydrogen atom.

This destai.llising effect would be expected to be in the

order 6-keto-⟩6-acetoxy-⟩6-desoxy-,[36] as was observed.

This effect of the C(6)-substituent has recently been

observed for other rearrangements leading to backbone—

rearranged products.[58,59] This same inductive effect

would also be expected to have an influence on the direction

of C-O fission, electronegative substituents favouring

C(9)-O cleavage as opposed to C(10)-O cleavage. Thus the

6-keto-epoxides (CXIIId,f) and 6β-acetoxy-epoxides (CXIIIa,b)

gave no products unambiguously derived from C(10)-O cleavage.

In contrast to the above epoxides the 6-desoxy-α-epoxide

(CXIIIg) gave the compound (CXXI) and the 6-desoxy-β-

-epoxide (CXIIIh) gave the compound (CXXXI), which are

both formed via initial C(10)-O cleavage. A double-

rearrangement is necessary for the formation of the diene

(CXXII). Although such a rearrangement is possible, it does

not seem very probable. It is known that some 9α-hydroxy-

-19-nor-10β-steroids and also some 10α-hydroxy-19-nor-9β-

steroids under the conditions of the Westphalen rearrangement,

or when treated with toluene-p-sulphonic acid in acetic

anhydride, give only the products of straightforward

dehydration.[60a]

Recently evidence for a stepwise carbonium ion

mechanism in the "backbone-rearrangement" of a

9β-cholestane derivative has been published.[103] The

"backbone-rearrangement" of the 9β,10β-epoxides (CXIIIb,f,h)

would support this mechanism, where the cis-8β-hydrogen atom

precludes any degree of concerted migration. Heterolysis

of the C(9)-O bond in the β-epoxides(CXIIIb,f,h) must give

a high degree of carbonium ion character at C(9). In

the case of the α-epoxides (CXIII a,d,g) there is the

possibility of some degree of concertedness in the C(9)-O

cleavage and 8β-hydrogen atom migration. This seems to be

indicated by the increased yields of the conjugated dienes

(CXV) and (CXVI) from the β-epoxides (CXIIIb,f,h) relative

to those from the α-epoxides (CXIIIa,d,g). The introduction

of the more electronegative C(6)-substituents also increases

the yields of the conjugated dienes (CXV) and (CXVI) from

both the α-epoxides (CXIIIa,d,g) and β-epoxides (CXIIIb,f,h).

This probably reflects the reduced migratory aptitude of

the C(8) hydrogen atom which allows a straightforward elimination

to compete with backbone rearrangement.

Discussion 2:-

8,9-Epoxy-3β-hydroxy-5α,8α-lanostane (CXXXIXa) [104] was

prepared by oxidation of 3β-hydroxy-5α-lanost-8-ene (CXL) [105]

with monoperphthalic acid. Acetylation of compound (CXXXIXa)

gave the 8α,9α-epoxide (CXXXIXb). [104] Both these epoxides

were found to be stable on recrystallisation from ethyl acetate

(c.f. reference 104). Treatment of the 8α,9α-epoxide

(CXXXIXb) with boron trifluoride or tin (IV) chloride gave

only the conjugated diene (CXLI). [106] The same result was

obtained by treating the 8α,9α-epoxide (CXXXIXb) with mineral

acid. [104] Lithium in ethylamine reduction (with or without

t-butanol) [104] gave the 9α-hydroxy-compound (CXLII), [104]

after acetylation and column chromatography. The by-product

of the reaction was found to be the diene (CXLI) and not, as

was previously reported, [104] the olefin (CXL). The

formation of the diene is probably due to the lithium cations

present in the reaction mixture acting as a Lewis acid. This

has been reported to occur during the lithium aluminium

hydride reduction of some epoxides. [107] Dehydration

of the 9α-hydroxy-compound (CXLII) with thionyl chloride in

pyridine gave the 9,11-olefin (CXLIII). [104] Similarly

treatment of the compound (CXLII) with sulphuric acid/acetic

anhydride/acetic acid, and with toluene-p-sulphonic acid/

acetic anhydride gave the 9,11-olefin (CXLIII) and no

rearrangement products. Oxidation of the olefin (CXLIII)

with monoperphthalic acid gave the 9α,11α-epoxide (CXLIVa).

CXXXIX

R
(a)   H
(b)   Ac

CXL

CXLI

CXLII

CXLIII

CXLIV
(a) 9α,11α
(b) 9β,11β

CXLV
(a) 9β H
(b) 9α H
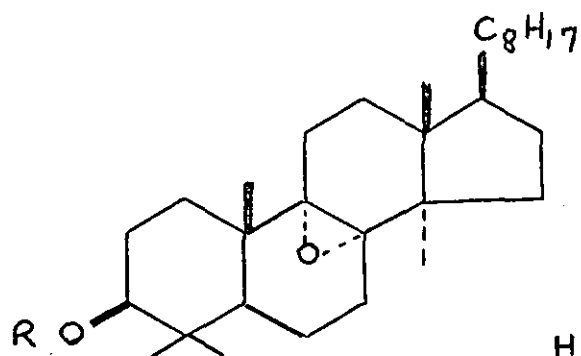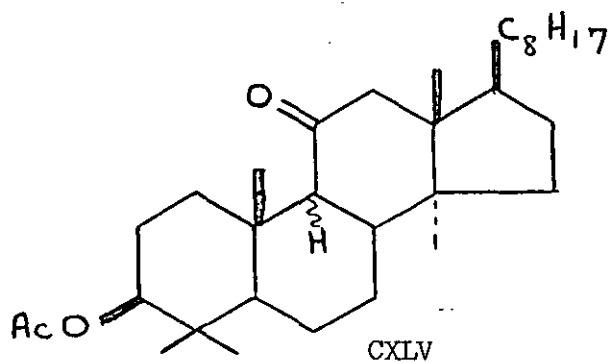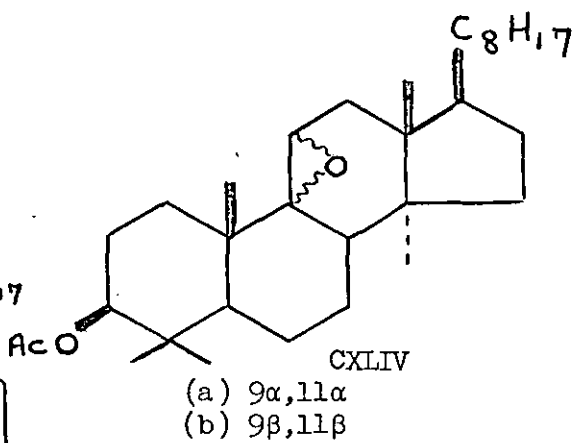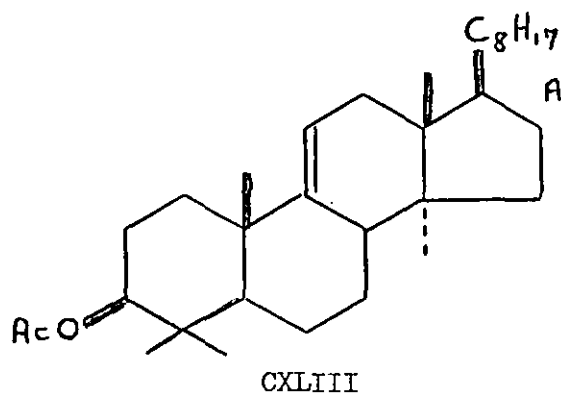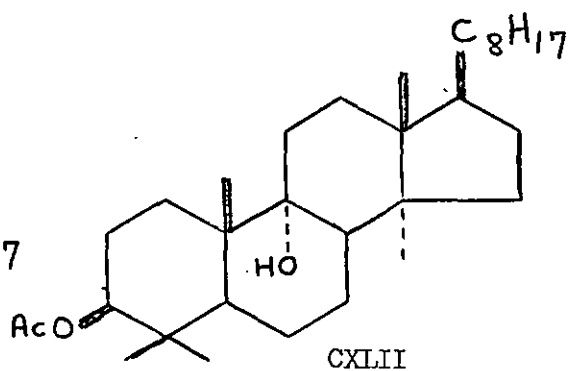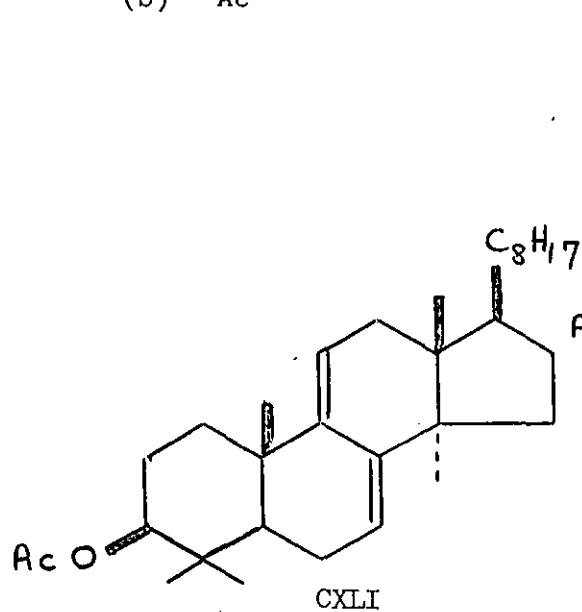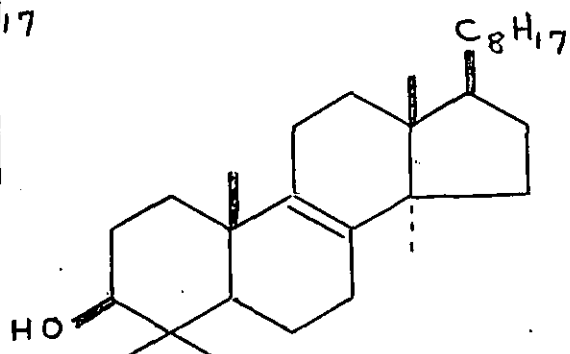
The appearance of the 11β-proton as a doublet (τ 7.04,

J (apparent) 4.8 Hz.) in the ^{1}H.n.m.r. spectrum of the

epoxide confirms the assigned 9α,11α-stereochemistry.

Treatment of the epoxide (CXLIVa) with boron trifluoride

or tin(IV) chloride in dry benzene gave the same reaction

mixture. Preparative t.l.c. of this mixture gave the 9β-11-ketone

(CXLVa) (35%) and the backbone-rearranged product (CXLVI) (45%).

The structure of the ketone was clear from the i.r.

spectrum (1713 cm.$^{-1}$) and from its conversion into the known

9α-11-ketone (CXLVb)[108] by successive treatment with base

and reactylation. The structure of the "backbone-compound"

(CXLVI) was indicated by the mass spectrum which shows a strong

peak (m/e 355) due to loss of side chain from the molecular

ion (m/e 462).[22] The 100 M.Hz. ^{1}H n.m.r. spectrum of the

compound (CXLVI) shows a single vinylic proton (τ 4.7) and

the C(21)H$_3$-doublet (τ 9.05; J. ca. 7 Hz.). This doublet

collapsed to a singlet on double irradiation 149 Hz. downfield,

confirming the $\triangle^{13,17}$-structure.[2] The i.r. and u.v.

spectra of the compound (CXLVI) were consistent with the

assigned structure. Treatment of the epoxide (CXLIVa) with

tin(IV) chloride in benzene has recently been reported[109]

to give only the ketone (CXLVa) (80%). The data reported

for the ketone (CXLVa) (m.p. 183-5°C., [α]$_D$+ 11°)[109] does not

agree with that obtained (m.p. 199-200°C., [α]$_D$+ 96°) in

the present work. The reasons for these differences are

not clear.

CXLVI

CXLVII

R
(a) Br
(b) OH

CXLVIII

R
(a) α ⁚ Br·,H
(b) = H₂

CXLIX

R
(a) H
(b) Ac

CL

CLI

CLII

CLIII
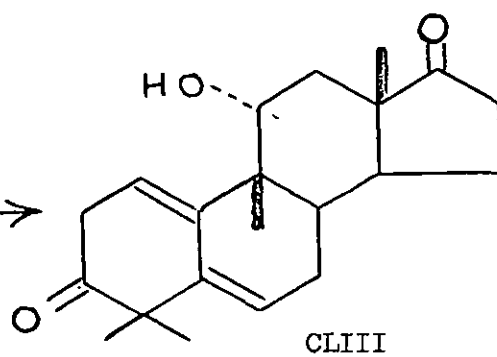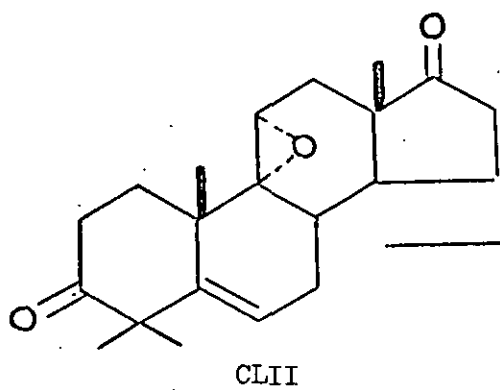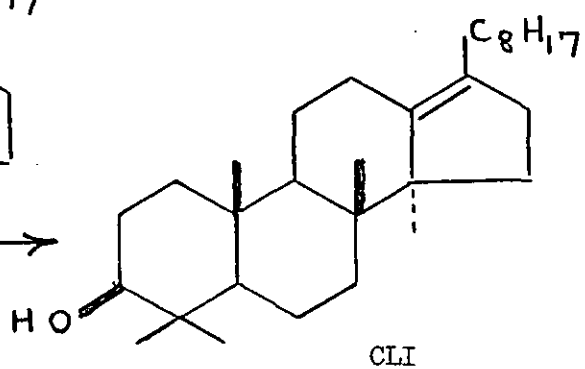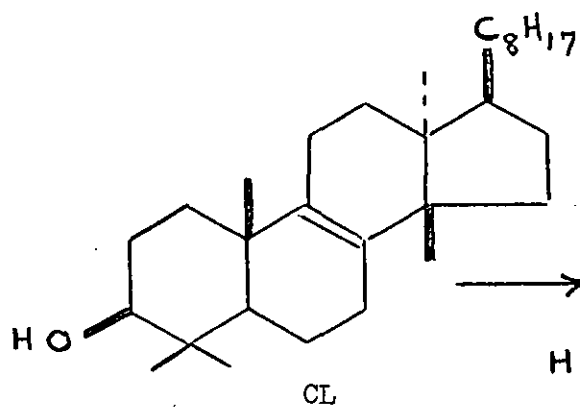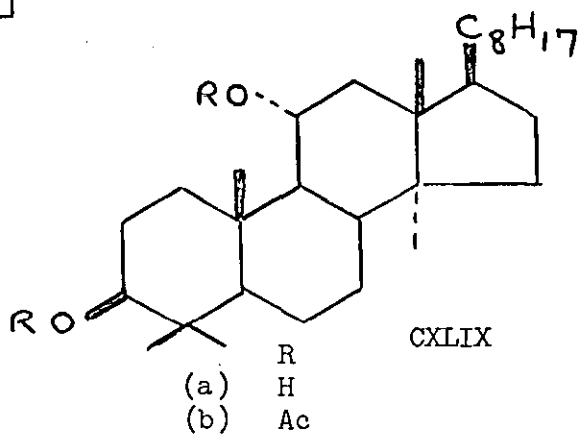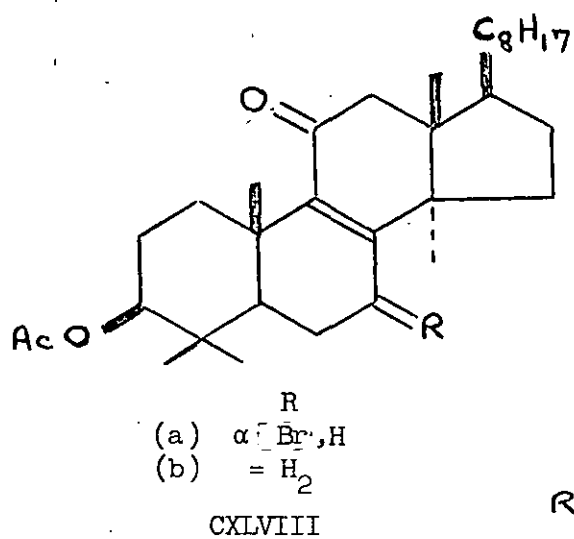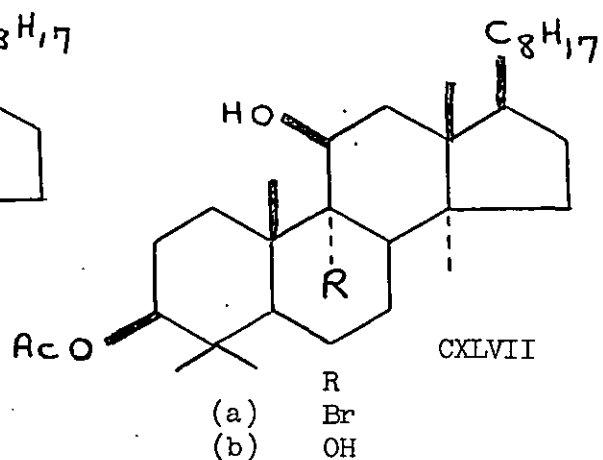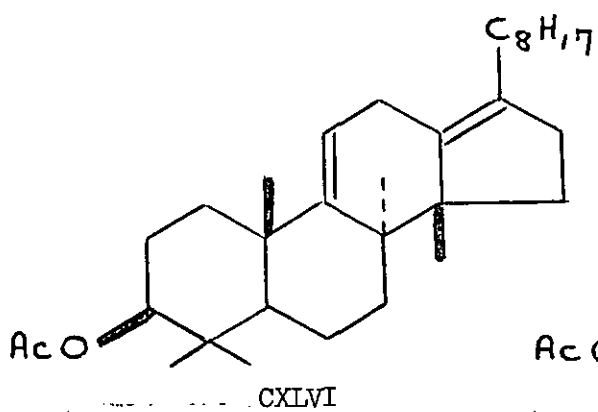
It was anticipated that the 9β,11β-epoxide (CXLIVb) might be prepared via the bromohydrin (CXLVIIa). The olefin (CXLIII) was therefore treated with N-bromoacetamide and perchloric acid ("HOBr") in peroxide free, aqueous dioxan.[110] A single product, the bromo-ketone (CXLVIIIa) was obtained. The i.r. spectrum of the bromo-ketone (CXLVIIIa) (1668 cm.$^{-1}$) is typical of an α,β-unsaturated ketone. The ^{1}H n.m.r. spectrum of the compound shows a signal at low field (τ 5.00; W$\frac{1}{2}$. ca. 7 Hz.) which is assigned to the equatorial 7β-methine proton. The u.v. spectrum ($\lambda_{max.}$ 267 n.m. $\varepsilon_{max.}$ 7,660) shows the $\lambda_{max.}$ shifted to a longer wavelength relative to the parent α,β-enone chromophore (CXLVIIIb) ($\lambda_{max.}$ 255).[108] Shifts to longer wavelengths of this magnitude have been recorded for the introduction of axial-γ-bromine atoms into other α,β-enone systems.[111] These shifts have been ascribed to second order effects due to partial overlap of the bromine p-orbitals with/the α,β-unsaturated chromophore.[111] Hydrogenolysis of the bromo-ketone (CXLVIIIa) using a palladium catalyst gave the α,β-unsaturated ketone (CXLVIIIb),[108] ($\lambda_{max.}$ 257 n.m. $\varepsilon_{max.}$ 9,370). There was some disagreement between the melting point recorded for the ketone (CXLVIIIb) (133-4°C.) and that in the literature[108] (119-20°C.). Accordingly the ketone was reduced using lithium in liquid ammonia[112] to give the diol (CXLIXa) from which the diacetate (CXLIXb) was obtained. Both these compounds have data in agreement with that in the literature.[113]

The failure of the olefin (CXLIII) to give the bromohydrin (CXLVIIa) is possibly due to a severe interaction in the transition state between the developing 9α-bromine atom and 14α-methyl group.

It was found that the 9α,11α-epoxide (CXLIVa) could be opened using periodic acid/dioxan or perchloric acid/methyl ethyl ketone[114] to give the diene (CXLI) but the 9α,11β-diol (CXLVIIb) was not obtained. Treatment of the epoxide with aqueous dioxan[115] gave recovered starting material. Attempts to introduce a 9α-chlorine atom by reaction of the olefin (CXLIII) with hypochlorous acid[116] or nitrosyl chloride[117] gave only recovered starting material.

The failure of the 8α,9α-epoxide (CXXXIXb) to rearrange to a $\triangle^{13,17}$-compound is probably due in part to the syn-conformation of the 14α-methyl and 8,9-epoxide groups. This requires the development of a full carbonium ion at C(8) for rearrangement to occur. This would allow diene formation to compete effectively, as in the case of the 9,10-epoxides studied[118] (Discussion 2). In contrast to this, the anti-conformation of the 8β-hydrogen atom and 9,11-epoxide group in the epoxide (CXLIVa) would allow a more concerted type of reaction which could compete effectively with elimination. Although the similar acid-catalysed rearrangement of dihydroeuphol (CL) to isoeuphenol (CLI) is well known,[119] the rearrangement of the 13β-methyl and 14α-methyl groups in the lanostane series has not been

previously reported. The failure of the 10β-methyl group

to migrate to C(9) in any of the above reactions is a

little surprising. Apparently the interaction between the

geminal C(4) dimethyl group and 10β-methyl group provides

insufficient driving force for this reaction to occur. As

stated previously (see Introduction) ApSimon et al. found

the generation of an allylic C(10) carbonium ion followed

by A-ring aromatisation provided insufficient driving force

for the 10β-methyl group to rearrange.[86] The rearrangement

of compound (CLII) to compound (CLIII) in good yield has

recently been reported.[120] The stabilisation of the

C(10) carbonium ion intermediate by the 5,6-double bond

provides sufficient additional driving force for this reaction.

These results have recently been reported by us in the

literature.[121]

Experimental:-

I.r. spectra were determined (for carbon tetrachloride
solutions unless otherwise stated) with Perkin-Elmer 237 and 257
spectrophotometers. U.v. spectra were determined (for hexane
solutions unless otherwise stated) with Unicam S.P.800 and
Uvispek spectrophotometers. ^{1}H N.m.r. spectra were
determined at 60 M.Hz., with a Perkin-Elmer R.10 spectrometer,
at 100 M.Hz. with a Varian H.A. 100 spectrometer or at
220 M.Hz. with a Varian H.R.220 spectrometer. Solutions
were in carbon tetrachloride unless otherwise stated.
Rotations were measured for chloroform solutions with a
Bendix polarimeter 143C. Mass spectra were determined
with A.E.I. M.S. 902 and M.S. 12 mass spectrometers. One
metre plates (0.5 m.m.) of Merck Kieselgel PF$_{254}$ were used
for preparative t.l.c. Column chromatography was carried
out using deactivated (Grade III) Camag neutral alumina.

Solutions were dried over anhydrous sodium sulphate and
solvents were removed in vacuo on a rotary evaporator.

The following standard experimental procedures were
adopted unless otherwise stated:-

Epoxidation.- The steroid was treated with a four molar
excess of monoperphthalic acid-ether solution (60 g./litre)
at room temperature overnight. The excess acid was removed
by washing the ether solution with a 2 N. sodium hydroxide
solution followed by washing with water. The solution was
dried and the solvent removed.

Hydrolysis.— A solution of the steroid in aqueous methanolic potassium hydroxide (5%) was refluxed for 30 minutes. The solution was cooled, poured into water and extracted with ether. The ether solution was washed well with water and dried, followed by removal of the solvent.

Acetylation.— The steroid was treated with an excess of acetic anhydride-pyridine (1:10) at room temperature overnight. The mixture was poured into water and extracted with ether. The ether was washed free of pyridine using dilute hydrochloric acid (2N.). This was followed by washing with a saturated sodium bicarbonate solution and water; after drying, the solvent was removed.

Oxidation.— Alcohols were oxidised using Jones reagent[20] (2 ml./1 g. steroid) in acetone (ca. 6 ml./1 g. steroid) for 5 minutes at $0°C.$. The mixture was poured into water and extracted with ether. The ether solution was washed with a saturated sodium bicarbonate solution followed by water. The solvent was removed after drying the solution.

Reaction of Epoxides with Boron trifluoride.—

The epoxide as a solution in sodium dried benzene (5% w./v.) was treated with boron trifluoride diethyletherate (1 ml./1 g. steroid) for the specified time at room temperature. The mixture was poured into a saturated sodium bicarbonate solution and was then extracted with ether. The ether extract was washed with water, and dried. The solvent was removed to give the crude product mixture.

Reaction of 5,6α-Epoxy-3β-hydroxy-5α-cholestane (XIVa).-

The epoxide (XIVa)[13] (1.7 g.) was reacted with boron trifluoride for 7 min. to give a crude product mixture. Preparative t.l.c. [eluting (x2) with benzene-ethylacetate (1:1)] gave the fluorohydrin (XVa) (34 mg.), m.p. 214-216° (from acetone), $[\alpha]_D$-7.5° (c. 0.25), τ (CDCl$_3$) 5.74 (d, J_{HF} ca. 50 Hz., 6-H), 5.92 (m, W$\frac{1}{2}$ ca. 24 Hz., 3-H), 8.90 (d, J_{HF} ca. 5 Hz., 10β-Me), 9.09 and 9.18 (side chain doublet), and 9.32 (s, 13β-Me) (lit.[14] m.p. 219-221°, $[\alpha]_D$+ 36°), the ketone (XVIa) (77 mg.), m.p. 143-144° (from aqueous methanol), $[\alpha]_D$- 5.5° (c. 0.5) (lit.[15] m.p. 142-143°, $[\alpha]_D$- 5.1°), the ketone (XVIb) (187 mg.), a gum, $[\alpha]_D$- 32° (c. 0.4), ν max. (CHCl$_3$) 3400 (OH), 1705 (C=O) cm.$^{-1}$, τ (CDCl$_3$) 5.89 (m, W$\frac{1}{2}$ ca. 8 Hz., 3-H), 9.09 and 9.18 (d, side chain methyls), 9.13 (s, 10β-Me), and 9.34 (s, 13β-Me) (lit.[16] m.p. 97°, $[\alpha]_D$-47°), the $\triangle^{13,17}$-compound (XVIIIa) (170 mg.), an amorphous solid, m.p. 147-149°, $[\alpha]_D$+ 38° (c. 0.8) (lit.[2] $[\alpha]_D$+ 37°), the slightly impure $\triangle^{9,10}$-compound (XVIIa) and a polar fraction (see later).

3β-Acetoxy-6β-fluoro-5-hydroxy-5α-cholestane (XVb).- The fluorohydrin (XVa) was acetylated to give the 3-acetate (XVb), m.p. 213-214° (from acetone/hexane), $[\alpha]_D$-26° (c.0.15), τ (CDCl$_3$) 4.80 (m, W$\frac{1}{2}$ ca. 24 Hz. 3-H), 5.73 (d, J_{HF} ca. 50 Hz., 6-H), 7.99 (s, OAc), 8.79 (d, J_{HF} ca. 6 Hz., 10β-Me), 9.10 and 9.19 (d, side chain methyls), and 9.32 (s, 13β-Me) (lit.[14] m.p. 212-214°, $[\alpha]_D$-22°).

3β-Acetoxy-5β-cholestan-6-one (XVId).-The ketone (XVIb) was

acetylated to give the 3-acetate (XVId), m.p. 137-138°

(from methanol), $[\alpha]_D$- 25° (c. 0.5) (lit.[16] m.p. 138°

$[\alpha]_D$- 26°).

$3\beta,6\alpha$-Diacetoxy-5-methyl-19-nor-5β-cholest-9(10)-ene (XVIIb).-

Acetylation of the $\triangle^{9,10}$-compound (XVIIa) and further

t.l.c. [ethyl acetate-benzene (1:3)] gave the diacetate

(XVIIb), a gum, $[\alpha]_D$+ 36° (c. 0.8), ε 7590 at 210 n.m.,

5000 at 215 n.m., and 2400 at 220 n.m., τ (CDCl$_3$) 4.90 (m,

W$\frac{1}{2}$ ca. 10 Hz., 3-H), 5.39 (q, J (apparent) ca. 11.2 and

3.1 Hz., 6-H), 8.03 (s, 2xOAc), 8.84 (s, 5β-Me), 9.10 and

9.19 (d, side chain methyls), and 9.24 (s, 13β-Me) (Found:

C, 76.7; H, 10.6. $C_{31}H_{50}O_4$ requires C, 76.5; H, 10.4%).

$3\beta,6\alpha$-Dihydroxy-5-methyl-19-nor-5β-cholest-9(10)-ene (XVIIa).-

Hydrolysis of the diacetate (XVIIb) gave the diol (XVIIa)

(overall yield 119 mg.), an amorphous solid, $[\alpha]_D$- 4.1°

(c. 1.0), τ (CDCl$_3$) 5.80 (m, W$\frac{1}{2}$ ca. 9 Hz., 3-H), 6.57 (q,

J (apparent) ca. 11 and 4 Hz., 6-H), 8.62 (s, 5β-Me), 9.09

and 9.18 (d, side chain methyls), and 9.23 (s, 13β-Me)

(Found: C, 80.2; H, 11.45. $C_{27}H_{46}O_2$ requires C, 80.5;

H, 11.5%).

Diketone (XVIIc).- Oxidation of the diol (XVIIa) gave the

diketone (XVIIc), a gum, $[\alpha]_D$- 46° (c. 0.8) (lit.[21] $[\alpha]_D$-

46°).

Diacetate (XVIIIc). Acetylation of the polar fraction

and further t.l.c. [ethyl acetate-benzene (1:5)] gave the

mono-acetate (XVIIIb), τ (CDCl$_3$) 5.49 (t, J (apparent) ca.

7.8 Hz., 6-H), and 5.95 (m, W$\frac{1}{2}$ ca. 9 Hz.,3-H). Acetylation

of the mono-acetate (XVIIIb) at 100° for 2 hr. gave the diacetate

(XVIIIc)(overall yield 290 mg.), a yellow oil,[α]$_D$+ 12°

(c. 0.8), τ (CDCl$_3$) 4.93 (m, W$\frac{1}{2}$ ca. 9 Hz.,3-H), 5.42 (t,

J (apparent) ca. 7.8 Hz.,6-H), 7.98 (s, 2 x OAc), 8.96 (s,

5β-Me), 9.01 (low-field branch of C(21)H$_3$-doublet), 9.11

(high field branch of C(21) H$_3$-doublet, 14β-Me, side chain),

and 9.23 (side chain) (lit.$^{(2)}$ [α]$_D$+ 14°)[see also reaction

of epoxide (XIVb)].

Diol (XVIIId).- Hydrolysis of the diacetate (XVIIIc) gave the

diol (XVIIId), m.p. 191-192.5° (from methanol), [α]$_D$+ 20°

(c.0.35) (lit.$^{(2)}$ m.p. 192-193°, [α]$_D$+ 21°).

Diketone (XVIIIe).- Oxidation of the diol (XVIIId) gave the

diketone (XVIIIe), a gum, [α]$_D$+ 34° (c. 0.4) (lit.$^{(2)}$[α]$_D$

+ 34°). The same diketone was obtained by oxidation of the

diol (XVIIIa).

Reaction of 5,6β-Epoxy-3β-hydroxy-5β-cholestane (XIVb).$^{(13)}$-

The epoxide (XIVb) (2.0 g.) was reacted for 7 min. with boron

trifluoride and gave a crude product which was separated by

preparative t.l.c. [eluting (x3) with ethyl acetate-benzene

(1:1)] to give the ketone (XVIa) (400 mg.), m.p. 154-156°

(from methanol), [α]$_D$- 5.2° (c. 1.9) (lit.$^{(15)}$ m.p. 142-3°,

[α]$_D$- 5.1°),and a polar fraction.

Acetate (XVIe).- Acetylation of the hydroxy-ketone (XVIa)

gave the 3-acetate (XVIe), m.p. 128-130°(from methanol),

$[\alpha]_D$-16° (c.1.1) (lit.,[15] m.p. 127-128°,$[\alpha]_D$- 15.5°).

Diacetate (XVIIIc).-Acetylation of the polar fraction at

100°C.for 2 hr. gave after t.l.c. on silver nitrate-impregnated

silica (10%) [ethyl acetate-benzene (1:10)] the diacetate

(XVIIIc) [2] (800 mg.), $[\alpha]_D$+ 11.3° (c. 1.06).

Reaction of 5,6α-Epoxy-3β-methoxy-5α-cholestane (XIVc).[28] -

The epoxide (XIVc) (1.0 g.) was reacted with boron trifluoride

for 5 min. to give a crude product. Preparative t.l.c. [ethyl

acetate-benzene (1:5)] gave five fractions of which four

appeared from spectroscopic data to be essentially homogeneous

and these were acetylated. T.l.c. of the four fractions gave

3β-methoxy-5β-cholestan-6-one (XVIc) (270 mg.), m.p. 108-

110°(from methanol), $[\alpha]_D$- 39° (c. 0.95),$\nu_{max.}$ 2835 and

1100 (OMe), 1708 (C=O) cm.$^{-1}$,τ 6.58 (m, W½ ca. 8 Hz., 3-H),

6.79 (s, OMe), 9.14 (d, side chain methyls), 9.19 (s, 10β-Me),

and 9.35 (s, 13β-Me) (Found: C, 80.75; H, 11.55. $C_{28}H_{48}O_2$

requires C, 80.7; H, 11.6%), 6α-acetoxy-3β-methoxy-5,14-

-dimethyl-18,19-bisnor-5β,8α,9β,10α,14β-cholest-13(17)-

ene (XVIIIf) (90 mg.), a gum, $[\alpha]_D$+ 51° (c. 0.5),$\nu_{max.}$

1733 (C=O), 1245 (C-O) and 1095 (OMe) cm.$^{-1}$, τ 5.44 (m,

W½. ca. 7 Hz., 6-H), 6.56 (m, W½ ca. 9 Hz., 3-H), 6.78 (s,

OMe), 8.02 (s, OAc), 8.92 (s, 5β-Me), 8.98 (lowfield branch

of C(21) H$_3$-doublet), 9.12 (high-field branch of C(21)H$_3$-

doublet, 14β-Me, side chain), and 9.22 (side chain) (the

C(21)H$_3$-doublet collapsed on double irradiation 88 Hz. downfield),

M (mass spectrum) 458.3757 (12% of base peak) ($C_{30}H_{50}O_3$requires

458.3760), base peak 285.2213 ($C_{20}H_{29}O$ requires 285.2218),

6α-acetoxy-3β-methoxy-5-methyl-19-nor-5β-cholest-9(10)-ene

(XVIId) (180 mg.), m.p. 71-73° (from methanol), $[\alpha]_D$+ 63°

(c. 0.7), ν max. 1740 (C=O), and 1240 (C-O) cm.$^{-1}$, τ 5.47

(q, J (apparent) ca. 10.3 and 2.6 Hz., 6-H), 6.52 (m, W$\frac{1}{2}$.

ca. 11 Hz., 3-H), 6.75 (s, OMe), 8.03 (s, OAc), 8.80 (s,

5β-Me), 9.14 (d, side chain methyls), and 9.22 (s, 13β-Me)

(Found: C, 78.75; H, 11.05. $C_{30}H_{50}O_3$ requires C, 78.55;

H, 11.0%), and 6α,9-epoxy-3β-methoxy-1(10→ 5)-abeo-5α-cholestane

(XXII) (70 mg.), $[\alpha]_D$+ 7.1° (c. 0.6), ν max. 2835, 1100 (OMe)

cm.$^{-1}$, τ (220 M.Hz.,CDCl$_3$) 6.17 (d, J (apparent) ca. 5.2 Hz.,

6-H), 6.24 (m, W$\frac{1}{2}$ ca. 14.6 Hz., 3-H), 6.73 (s, OMe), 9.09

(d, J (apparent) ca. 7.5 Hz., 10β-Me), 9.13 (d, side chain

methyls), and 9.37 (s, 13β-Me), M (mass spectrum) 416.3657

($C_{28}H_{48}O_2$ requires 416.3654) (Found: C, 80.25; H, 11.7.

$C_{28}H_{48}O_2$ requires C, 80.7; H, 11.6%).

Ketone (XVIIe).- Hydrolysis of the $\triangle^{9,10}$-compound (XVIId)

gave the alcohol (XVIIf), ν max. 3640 and 3480 (OH) cm.$^{-1}$,

τ 6.6 (m, 3- and 6-H), 6.80 (s, OMe), 8.82 (s, 5β-Me), 9.18

(d, side chain), and 9.29 (s, 13β-Me), which on oxidation gave

the ketone (XVIIe), m.p. 64-66° (from methanol), $[\alpha]_D$- 8.0°

(c. 0.30) (lit.,[28] m.p. 65°, $[\alpha]_D$- 7.8°).

3,6-Dioxo-14-methyl-1(10→ 5)-abeo-18-nor-5α,8α,9β,14β-

cholest-13(17)-ene. (XXIV).- The epoxy-spiran (XXII) (150 mg.)

as a solution in acetic acid (6 ml.) and acetic anhydride

(2 ml.) was treated with boron trifluoride (1.1 ml.) for 12 hr.

at 0°. Ether was added and the mixture was poured into 2 N.

sodium hydroxide solution. The ether extract was washed

with water, dried, and the solvent removed. The crude extract

was hydrolysed and oxidised to give a crude mixture. Preparative

t.l.c. (benzene) gave the <u>dioxo-spiran</u> (XXIV)(20 mg.), a gum,

$\nu_{max.}$ 1750 (3-C=O), and 1715 (6-C=O) cm.$^{-1}$, τ 9.01

(low-field branch of C(21)H_3-doublet), 9.08 (high-field branch

of C(21)H_3, 14β-Me), and 9.16 (d, side chain methyls) (Double

irradiation 83 Hz. downfield caused the C(21) H_3-doublet to

collapse to a shoulder on the 14β-methyl signal), M (mass

spectrum) 398.3187 ($C_{27}H_{42}O_2$ requires 398.3185), base peak

285.1849 ($C_{19}H_{25}O_2$ requires 285.1854).

<u>Reaction of a Mixture of Cyclohexanol and Epoxide</u> (XIVd).-

A mixture of the epoxide (1.0 g.) and cyclohexanol (0.23 g.)

was treated with boron trifluoride ether complex (300 mg.,

<u>ca</u>. 1 mol. with respect to steroid) under the usual conditions

for 5 min.. Preparative t.l.c. [ethyl acetate-benzene (1:10)]

allowed the isolation of the major product, the fluorohydrin

(XVb)[14] (400 mg.), m.p. 213-214°, $[\alpha]_D$-20° (c.0.84).

Variation of the quantity of boron trifluoride (0.1, 1.5,

and 10 mol.) did not appear (t.l.c.) to change the mixture

of products.

<u>Reaction of 3β-Acetoxy-5,6α-epoxy-5α-androstan-17-one</u> (XXVIIIa).-

The epoxide[41] (1.2 g.) was reacted with boron trifluoride

for 5 min.. The crude product was separated by preparative

t.l.c. [ethyl acetate-benzene(1:3)] and gave the fluorohydrin

(XXIXa) (812 mg.), m.p. 165-166° (from methanol), $[\alpha]_D$+ 24(c.1.0),

$\mathcal{V}_{max.}$ (CHCl$_3$) 3620 and 3450 (OH), 1740 (acetate and

17-C=0), and ca. 1250 (C-0) cm.$^{-1}$, τ (CDCl$_3$) 4.90 (m,

W$\frac{1}{2}$ ca. 20 Hz., 3-H), 5.71 (d, J$_{HF}$ ca. 50 Hz., 6-H), 8.00

(s, OAc), 8.90 (d, J ca. 5 Hz., 10β-Me), and 9.13 (s,

13β-Me) (lit.$_{,}$[122] m.p. 160°, [α]$_D$+ 15.6), the epoxide

(XXVIIIa) (78 mg.), and a polar material.

3β,6α-Diacetoxy-5-methyl-19-nor-5β-androst-9(10)-en-17-one

(XXXb).- Acetylation and further t.l.c. of the polar material

from above gave the diacetate (XXXb) (211 mg.), a gum,

[α]$_D$+ 94° (c. 0.85), $\mathcal{E}$ 5380 at 215 n.m., $\mathcal{V}_{max.}$ (CHCl$_3$)

1735 (acetate and 17 C=0), and 1240 (C-0) cm.$^{-1}$, τ (CDCl$_3$)

4.86 (m, W$\frac{1}{2}$ ca. 10 Hz., 3-H), 5.32 (q, J (apparent) ca. 11

and 4 Hz., 6-H), 7.95 (s, 2 x OAc), 8.76 (s, 5β-Me), and

9.03 (s, 13β-Me) (Found: C, 70.89; H, 8.38. C$_{23}$H$_{32}$O$_5$

requires C, 71.10; H, 8.30%).

Diketone (XXXc).- The diacetate (XXXb) was hydrolysed and

oxidised to give the 3,6-diketone (XXXc), m.p. 175-176° (from

benzene-petrol), $\mathcal{V}_{max.}$ 1740 (17-C=0), and 1718 (3,6-C=0) cm.$^{-1}$

(lit.$_{,}$[42] m.p. 175-177°).

Reaction of 5,6α-Epoxy-3β-hydroxy-5α-androstan-17-one (XXVIIIb).-

The epoxide (XXVIIIb)[41] (600 mg.) was reacted as a

saturated solution (ca. 1.2%) in benzene with boron trifluoride

for 7 min.. The crude product was acetylated. Preparative

t.l.c. [ethyl acetate-benzene (1:3)]gave the $\triangle^{9,10}$-compound

(XXXb) (244 mg.) and an inseparable mixture of three products

(455 mg.). From the methine proton signals in the ^{1}H n.m.r.

spectrum of the mixture the percentage yields of the fluorohydrin

(XXIXa) (25%), the ketone (XXXIa) (18.5%) and the epoxide

(XXVIIIb) (ca. 2%) were estimated. Preparative t.l.c. of the

mixture [benzene-ethyl acetate (1:1)] gave some pure fluorohydrin

(XXIXa). The mixture was hydrolysed to give a mixture of two

products (by t.l.c.). Treatment of this mixture with periodic

acid in refluxing acetone[43] for 30 min. on work up gave a

mixture of two products. Preparative t.l.c. [eluting(x 2)with

benzene-ethyl acetate (1:1)] gave the ketone (XXXIb), m.p.

205-207° (from methanol), $[\alpha]_D$+ 30° (c. 0.35) (lit.,[44] m.p.

204-207°, $[\alpha]_D$+ 33), and the triol (XXIXb), m.p. 296-298°

(from acetone) (lit.,[45] m.p. 301-302).

Attempted Isomerisation of the $\triangle^{9,10}$-Compound (XXXb).-

Treatment of the $\triangle^{9,10}$-compound (XXXb) with boron

trifluoride in benzene as usual, for 18 hr., on work up

gave only recovered starting material.

Reaction of 5,6β-Epoxy-3β-hydroxy-5β-androstan-17-one (XXVIIIc).[41]

- The epoxide (XXVIIIc) (0.6 g.) was reacted with boron

trifluoride as a saturated solution (ca. 1%) for 7 min..

Preparative t.l.c. [benzene-ethyl acetate (1:1)] of the

crude product gave three fractions. Further t.l.c. [chloroform-

methanol (19:1)] of one fraction gave the ketone (XXXIb)[44]

(91 mg.), ν max. (CHCl$_3$) 3610 and 3460 (OH), 1740 (17-C=O),

and 1715 (6-C=O) cm.$^{-1}$, τ (CDCl$_3$) 6.42 (m, W$\frac{1}{2}$ ca. 24 Hz.,

3-H), 9.12 (s, 10β-Me), and 9.22 (s, 13β-Me), and a second fraction.

This was acetylated and recrystallised to give 3β,6β-diacetoxy-

-5-fluoro-5α-androstan-17-one (XXIXd) (217 mg.), m.p. 248°

(from methanol), $[\alpha]_D$+ 7.1° (c. 0.71), τ (CDCl$_3$) 4.60-5.40

(m, 3,6-H), 7.91 (s, OAc), 7.99 (s, OAc), 8.82 (s, 10β-Me), and

9.10 (s,13β-Me) (Found: C, 67.78; H, 8.24. $C_{23}H_{33}O_5F$

requires C, 67.64; H, 8.14%). A second fraction was acetylated,

and further t.l.c. [ether-petrol (1:1)] gave 3β,6β-diacetoxy-

5-methyl-19-nor-5β-androst-1(10)-en-17-one (XXXIIa) (39 mg.),

m.p. 220-222° (from methanol), $[\alpha]_D+ 16°$ (c. 0.31), ν max.

(CHCl$_3$) 1735 (OAc and 17 C=O), and ca. 1240 (C-O) cm.$^{-1}$, τ

(CDCl$_3$) 4.56-5.30 (m, 1, 3, 6-H), 7.92 (s, OAc), 7.98 (s,

OAc), 8.75 (s, 5β-Me), and 9.11 (s, 13β-Me) (Found: C, 71.11; H,

8.34. $C_{23}H_{32}O_5$ requires C, 71.10; H, 8.30%). The third

fraction (120 mg.) was an inseparable polar mixture.

Diketone (XXXIIb).- The diacetate (XXXIIa) was hydrolysed and

oxidised to give the diketone (XXXIIb), a gum, ν max. 1745

(17-C=O), and 1720 (3,6-C=O) cm.$^{-1}$, τ 4.5 (m, W½ ca. 12 Hz.,

1-H), 8.76 (s, 5β-Me), and 9.12 (s, 13β-Me).

Attempted Isomerisation of the Diketone (XXXIIb).- The diketone

(XXXIIb) (12 mg.) in ethanol (0.6 ml.) was refluxed for 1 hr.

with ethanolic potassium hydroxide (0.1 ml., 30%). Work up

gave a mixture (by t.l.c.), which was not further investigated.

Treatment of the Fluorohydrin (XXIXd) with Base.-

The fluorohydrin (XXIXd) (100 mg.) was heated under

reflux in methanolic potassium hydroxide solution (5%) for

30 min. and poured into water. Extraction with ether gave the

hydroxy-epoxide (XXVIIIc) (71 mg.) identical with an authentic

sample.

5,6α-Epoxy-3β-methoxy-5α-androstan-17-one (XXVIIId).- 3β-Methoxy-

-androst-5-en-17-one[48](3.0 g.) was epoxidised to give the

<u>5,6α-epoxide</u> (XXVIIId) (3.0 g.), m.p. 167-169° (from methanol),

$[\alpha]_D$- 18.5°(c. 0.6), $\nu_{max.}$ 2830, 1095 (OMe) and 1735 (17

C=O) cm.$^{-1}$, τ (CDCl$_3$) 6.6-6.95 (m, 3-H), 6.69 (s, OMe),

7.07 (d, J (apparent) <u>ca</u>. 4 Hz., 6-H), 8.93 (s, 10β-Me), and

9.19 (s, 13β-Me) (Found: C, 75.27; H, 9.28.   C$_{20}$H$_{30}$O$_3$

requires C, 75.43; H, 9.50%).

<u>Reaction of 5,6α-Epoxy-3β-methoxy-5α-androstan-17-one</u> (XXVIIId).-

The epoxide (XXVIIId) (2.0 g.) was reacted with boron trifluoride

for 5 min.. Preparative t.l.c. [benzene-ethyl acetate (1:1)]

gave two fractions which were acetylated. Further t.l.c.

[benzene-ethyl acetate (10:1)] of these fractions gave

<u>6α-acetoxy-3β-methoxy-5-methyl-19-nor-5β-androst-9(10)-en-17-one</u>

(XXXd) (400 mg.), m.p. 152° (from methanol), $[\alpha]_D$+ 136°(c.076)$_,$

$\mathcal{E}$ 4,600 at 215 n.m., $\nu_{max.}$ 2830, 1090 (OMe), 1745 (acetate

and 17-C=O), and 1240 (C-O) cm.$^{-1}$, τ (CDCl$_3$) 5.33 (q,

J (apparent) <u>ca</u>. 10 and 4 Hz., 6-H), 6.47 (m, $W\frac{1}{2}$ <u>ca</u>. 12 Hz.,

3-H), 6.71 (s, OMe), 7.98 (s, OAc), 8.76 (s, 5β-Me), and 9.04

(s, 13β-Me) (Found: C, 72.85; H, 8.85.   C$_{22}$H$_{32}$O$_4$ requires

C, 73.30; H, 8.95%), <u>6β-fluoro-5-hydroxy-3β-methoxy-5α-androstan-</u>

<u>-17-one</u> (XXIXe) (269 mg.), m.p. 223-225° (from methanol),

$[\alpha]_D$+ 42°(c. 0.75), $\nu_{max.}$ (CHCl$_3$) 3610 and 3440 (OH),

2830, 1095 (OMe), and 1740 (C=O) cm.$^{-1}$, τ (CDCl$_3$) 5.71

(d, J$_{HF.}$ <u>ca</u>. 50 Hz., 6-H), 6.40 (m, $W\frac{1}{2}$ <u>ca</u>. 22 Hz.,3-H),

6.67 (s, OMe), 8.87 (d, J$_{HF.}$ <u>ca</u>. 5 Hz., 10β-Me), and 9.12

(s, 13β-Me) (Found: C, 71.33; H, 9.07.   C$_{20}$H$_{31}$O$_3$F requires

C, 70.99; H, 9.24%), <u>3β-methoxy-5β-androstan-6,17-dione</u> (XXXIc)

(414 mg.), m.p. 163-164° (from methanol),$[\alpha]_D$ + 6.7° (c. 0.76),

$\nu_{max.}$ 2830, 1095 (OMe), 1750 (17 C=O), and 1715 (6 C=O)

cm.$^{-1}$, τ 6.59 (m, $W\frac{1}{2}$ ca. 8 Hz., 3-H), 6.78 (s, OMe), and

9.14 (s, 10β,13β-methyls) (Found: C, 75.07; H, 9.39.

$C_{20}H_{30}O_3$ requires C, 75.43; H, 9.50%), and the epoxide

(XXVIIId) (85 mg.).

Reaction of 3β-Acetoxy-5,6α-epoxy-5α-pregnan-20-one

(XXXIIIa).[41] - The epoxide (XXXIIIa) (1.65 g.) was reacted

with boron trifluoride for 10 min.. The crude product was

separated by preparative t.l.c. [benzene-ethyl acetate (3:1)]

and gave the fluorohydrin (XXXIVa) (1.26 g.), m.p. 222-224°

(from methanol), $[\alpha]_D$+ 43°(c. 0.38), τ (CDCl$_3$) 4.90 (m,

$W\frac{1}{2}$ ca. 22 Hz., 3-H), 5.78 (d, $J_{HF.}$ ca. 50 Hz., 6-H), 7.90

(s, CH$_3$CO-), 8.00 (s, CH$_3$CO-), 9.11 (d, J_{HF} ca. 4 Hz., 10β-Me),

and 9.39 (s, 13β-Me) (lit.,[14] m.p. 223-224°, $[\alpha]_D$+ 42°),

the epoxide (XXXIIIa) (218 mg.) and a polar fraction.

Diacetate (XXXVb). The above fraction was acetylated.

Preparative t.l.c. [benzene-ethyl acetate (19:1)] gave

3β,6α-diacetoxy-5-methyl-19-nor-5β-pregn-9(10)-en-20-one

(XXXVb) (140 mg.), m.p. 118-119° (from methanol), $[\alpha]_D$

+ 136° (c. 0.5), ε 5,350 at 215 n.m., $\nu_{max.}$ 1740

(acetate C=O), 1712 (C=O), and 1235 (C-O) cm.$^{-1}$, τ (CDCl$_3$)

4.98 (m, $W\frac{1}{2}$ ca. 10 Hz., 3-H), 5.44 (q, J (apparent) ca.

11 and 4 Hz., 6-H), ca. 7.99 (m, 3x CH$_3$CO-), 8.80 (s, 5β-Me),

and 9.29 (s, 13β-Me) (Found: C, 71.83; H, 8.90.

$C_{25}H_{36}O_5$ requires C, 72.08; H, 8.71%).

Diketone (XXXVc).- The diacetate (XXXVb) (100 mg.) on

hydrolysis and oxidation gave the diketone (XXXVc) (50

mg.), m.p. 168-169° (from ethanol), $[\alpha]_D$+ 6°(c. 0.8) (lit.,

(51) m.p. 167-169°, $[\alpha]_D$+ 7.8°).

Reaction of 5,6α-Epoxy-3β-hydroxy-5α-pregnan-20-one

(XXXIIIb).[41] - The epoxide (XXXIIIb) (1.4 g.) was treated

with boron trifluoride for 7 min.. The crude product was

acetylated. Preparative t.l.c. [benzene-ethyl acetate

(3:1)] gave three fractions. Two fractions were further

separated by t.l.c. [benzene-ethyl acetate (10:1)] and gave

the fluorohydrin (XXXIVa) (129 mg.), 3β-acetoxy-5β-pregnan-

-6,20-dione (XXXVIa) (439 mg.), m.p. 111-112° (from petroleum

ether), $[\alpha]_D$+ 13.8° (c. 0.72), $\nu_{max.}$ 1740 (acetate C=O),

1710 (6,20-C=O), and 1240 (C-O) cm.$^{-1}$, τ 5.02 (m, W½ ca.

8 Hz., 3-H), 7.99 (s, CH_3CO-), 8.01 (s, CH_3CO-), 9.14 (s,

10β-Me), and 9.44 (s, 13β-Me) (Found: C, 73.84; H, 9.22.

$C_{23}H_{34}O_4$ requires C, 73.76; H, 9.15%), and the $\triangle^{9,10}$-

compound (XXXVb) (517 mg.). The third fraction (490 mg.)

of polar material was not further investigated.

Reaction of 5,6β-Epoxy-3β-hydroxy-5β-pregnan-20-one

(XXXIIIc).[41] - The epoxide (2.0 g.) was treated with

boron trifluoride for 5 min.. The crude product was

acetylated and preparative t.l.c. [benzene-ethyl acetate

(10:1)] gave 3β,6β-diacetoxy-5-fluoro-5α-pregnan-20-one

(XXXVII) (1.25 g.), m.p. 221-222° (from acetone), [α]

0° (c. 0.77), $\nu_{max.}$ 1740 (acetate C=O), 1710 (C=O) and

1248 (C-O) cm.$^{-1}$, τ (CDCl$_3$) 4.6 - 5.4 (m, 3,6-H),

7.93, 7.96, 8.03 (s, 3 x CH$_3$CO-),8.87 (s, 10β-Me), and

9.38 (s, 13β-Me) (Found: C, 68.87; H, 8.34. C$_{25}$H$_{37}$O$_5$F

requires C, 68.71; H, 8.54%), and the ketone (XXXVIb)

(518 mg.), m.p. 155-156° (from aqueous methanol), [α]$_D$+

26° (c. 0.57) (lit.[53] m.p. 155-156°). Some highly polar

material (450 mg.) was not further investigated.

Ketone (XXXVId).- The acetoxy-ketone (XXXVIb) was hydrolysed

to give the hydroxy-ketone (XXXVId), m.p. 185-187° (from

ethyl acetate), ν $_{max.}$ (CHCl$_3$) 3620 and 3470 (OH), and 1710

(6, 20 - C=O) cm.$^{-1}$, τ (CDCl$_3$) 6.40 (m, W½ ca. 23 Hz., 3-H),

7.90 (s, CH$_3$CO-), 9.25 (s, 10β-Me), and 9.39 (s, 13β-Me)

(lit.[53] m.p. 186-187°).

5,6α-Epoxy-3β-methoxy-5α-pregnan-20-one (XXXIIId).-

3β-Methoxy-pregn-5-en-20-one[54] (2.5 g.), was epoxidised

to give the α-epoxide (XXXIIId) (2.5 g.), m.p. 146-148°

(from ethyl acetate), [α]$_D$ 0° (c. 0.67), $\nu$$_{max.}$ 2830, 1095

(OMe), and 1708 (C=O) cm.$^{-1}$, τ 6.55-7.00 (m, 3-H), 6.80

(s,OMe), 7.25 (d, J (apparent) ca. 4 Hz., 6-H), 8.06 (s,

CH$_3$CO-), 8.99 (s, 10β-Me), and 9.49 (s, 13β-Me) (Found:

C, 76.21; H, 9.78 . C$_{22}$H$_{34}$O$_3$ requires C, 76.26; H, 9.89%).

Reaction of 5,6α-Epoxy-3β-methoxy-5α-pregnan-20-one (XXXIIId).-

The epoxide (XXXIIId) (3.0 g.) was reacted with boron trifluoride

for 5 min.. Preparative t.l.c. [benzene-ethyl acetate (10:1)]

of the mixture gave two fractions. The first fraction was

further separated by t.l.c. [ether-petrol (3:2)] and the

fractions acetylated. Further t.l.c. of these fractions

gave 6α-acetoxy-3β-methoxy-5-methyl-19-nor-5β-pregn-9(10)-en-20-

-one (XXXVd) (680 mg.), a gum, $[\alpha]_D$+ 97° (c. 0.7), ϵ 5,200

at 215 n.m., ν max. 2820, 1090 (OMe), 1730 (acetate C=O),

1705 (C=O), and 1235 (C-O) cm.$^{-1}$, τ 5.47 (q, J (apparent)

ca. 11 and 4 Hz., 6-H), 6.52 (m, W$\frac{1}{2}$ ca. 11 Hz., 3-H), 6.76

(s, OMe), 8.00, 8.04 (s, 2 x CH$_3$CO-), 8.81 (s, 5β-Me), and 9.30

(s, 13β-Me), M (mass spectrum), 388.2562 (C$_{24}$H$_{36}$O$_4$ requires

388.2613), 6β-fluoro-5-hydroxy-3β-methoxy-5α-pregnan-20-one

(XXXIVb) (236 mg.), m.p. 190-191° (from methanol), $[\alpha]_D$+

41°(c. 0.8), ν max. (CHCl$_3$) 3600, 3450 (OH), 3830, 1095

(OMe), and 1700 (C=O) cm.$^{-1}$, τ (CDCl$_3$) 5.77 (d, J$_{HF}$. ca.

50 Hz., 6-H), 6.3-6.7 (m, 3-H), 6.68 (s, OMe), 7.91 (s, CH$_3$CO-),

8.90 (d, J$_{HF}$. ca. 5 Hz., 10β-Me), and 9.37 (s, 13β-Me) (Found:

C, 72.04; H, 9.76. C$_{22}$H$_{35}$O$_3$F requires C, 72.02; H, 9.63%),

and 6α-acetoxy-3β-methoxy-1(10 → 5)-abeo-5α-pregn-9(10)-en-

-20-one (XXXVIII) (98 mg.), a gum, $[\alpha]_D$+ 62.5° (c. 0.92),

ϵ 6520 at 215 n.m., ν max. 2825, 1095 (OMe), 1735 (acetate

C=O), 1708 (C=O), and 1240 (C-O) cm.$^{-1}$, τ 5.33 (q, J (apparent)

ca. 11 and 4 Hz., 6-H), 6.28 (m, W$\frac{1}{2}$ ca. 14 Hz., 3-H), 6.82

(s, OMe), 8.00, 8.04 (2 x CH$_3$CO-), 8.32 (s, 10-Me), and 9.31

(s, 13β-Me), M (mass spectrum) 388.2608 (C$_{24}$H$_{36}$O$_4$ requires

388.2613). The second fraction was separated by t.l.c.

[ether-petrol (2:3)] to give 6α,9-epoxy-3β-methoxy-1(10→ 5)-

abeo-5α-pregnan-20-one (XXXIX) (55 mg.), a gum, $[\alpha]_D$+ 59.6°

(c. 0.71), ν max. 2835, 1105 (OMe), and 1708 (C=O) cm.$^{-1}$

τ (100 M.Hz., CDCl$_3$) 6.17 (d, J ca. 6 Hz., 6-H), 6.26 (m,

W$\frac{1}{2}$ ca. 18 Hz., 3-H), 6.75 (s, OMe), 7.91 (s, CH$_3$CO-), 9.15

(d, J $\underline{ca}$. 7 Hz., 10β-Me), and 9.44 (s, 13β-Me) (Double

irradiation 66 Hz. downfield caused the 10β-methyl doublet

to collapse) (Found: C, 75.82; H, 9.95. $C_{22}H_{34}O_3$ requires

C, 76.26; H, 9.89%), and 3β-methoxy-5β-pregnan-6,20-dione

(XXXVIc) (399 mg.), m.p. 172-173° (from methanol), $[\alpha]_D$- 2.5°

(c. 1.1), ν max. 2835, 1105 (OMe), and 1710 (C=O) cm.$^{-1}$,

τ 6.58 (m, W½ $\underline{ca}$. 8 Hz., 3-H), 6.79 (s, OMe), 7.98 (s,

CH_3CO-), 9.19 (s, 10β-Me), and 9.42 (s, 13β-Me) (Found: C,

76.35; H, 9.82. $C_{22}H_{34}O_3$ requires C, 76.26; H, 9.89%).

3β-Hydroxy-19-methyl-cholest-5-ene (XLVIIIa).- A 2.0 M hexane

solution of n-butyllithium (26 ml.) was added to a suspension

of methyltriphenylphosphonium iodide (22 g.) in dry

benzene (200 ml.) and the mixture stirred under nitrogen for

2 hr. . 3β-Hydroxy-19-oxo-cholest-5-ene (XLVI) [61] (8.1 g.)

dissolved in dry benzene (200 ml.) was added slowly. The

mixture was stirred overnight at room temperature and then

refluxed for 6 hr. . After cooling, the mixture was poured into

water, extracted with ether and the ether extracts dried and

evaporated. The resulting oil after column chromatography

(eluting with benzene, followed by 10% ether-benzene) gave the

10β-ethenyl steroid (XLVII) [60a] (5.6 g.). An ethyl acetate

solution of the steroid (XLVII) was stirred with a 10% palladium

on charcoal catalyst, in an atmosphere of hydrogen at room

temperature until the uptake of hydrogen had ceased. The solution

was filtered and evaporated and the resulting oil, recrystallised

from acetone-methanol, gave the 19-methyl-steroid (XLVIIIa)

(5.7 g.), m.p. 86-88°, $[\alpha]_D$-23° (c. 0.60), τ 4.55 (m, W½

$\underline{ca}$. 8 Hz., 6-H), 6.61 (m, $W\frac{1}{2}$ $\underline{ca}$. 26 Hz., 3-H), and 9.31 (s,

13β-Me) (Found: C, 84.03; H, 11.56. $C_{28}H_{48}O$ requires

C, 83.93; H, 1208%).

<u>5,6α-Epoxy-3β-hydroxy-19-methyl-5α-cholestane</u> (XLVa).-

Epoxidation of the 19-methyl-steroid (XLVIIIa) (6.0 g.) gave

as the sole product, the $\underline{\alpha\text{-epoxide}}$ (XLVa) (4.9 g.), m.p.

74-75° (from methanol), $[\alpha]_D$- 43° (c. 0.64), ν max. 3640

and $\underline{ca}$. 3450 (OH) cm.$^{-1}$, τ 6.2 (m, $W\frac{1}{2}$ $\underline{ca}$. 24 Hz., 3-H),

7.19 (d, J $\underline{ca}$. 3.1 Hz., 6-H), and 9.35 (s, 13β-Me) (Found:

C, 81.1; H, 11.3. $C_{28}H_{48}O_2$ requires C, 80.7; H, 11.6%).

<u>3β-Acetoxy-5,6α-epoxy-19-methyl-5α-cholestane</u> (XLVb).-

The hydroxy-epoxide (XLVa) (2.0 g.) was acetylated and gave

the <u>acetoxy-α-epoxide</u> (XLVb) (1.5 g.), m.p. 67-68° (from

methanol), $[\alpha]_D$- 40° (c. 0.7), $\nu_{max.}$ 1740 (C=O), and 1245

(C-O) cm.$^{-1}$, τ 5.2 (m, $W\frac{1}{2}$ $\underline{ca}$. 26 Hz., 3-H), 7.18 (d, J

$\underline{ca}$. 3.1 Hz., 6-H), 8.12 (s, OAc), and 9.37 (s, 13β-Me)

(Found: C, 78.5; H, 10.6. $C_{30}H_{50}O_3$ requires C, 78.55;

H, 11.0%).

<u>3β-Methoxy-19-methyl-cholest-5-ene</u> (XLVIIIb).[60b]- The

hydroxy-olefin (XLVIIIa) (500 mg.) in trimethylorthoformate

(5 ml.) was stirred at room temperature and perchloric acid

(0.5 ml., 60% w/v.) was slowly added. The stirring was continued

for a further 15 min. and the mixture poured into a sodium

bicarbonate solution and extracted with ether. The extract was

dried and the solvent removed to give the methyl-ether (XLVIIIb)

(450 mg.), m.p. 80-82° (from methanol),$[\alpha]_D$- 51° (c. 0.46),

(lit.,[60b] m.p. 81-82°, [α]$_D$-53°).

<u>5,6α-Epoxy-3β-methoxy-19-methyl-5α-cholestane</u> (XLVc).-

The methoxy-olefin (XLVIIIb) (1.8 g.) was epoxidised to

give the <u>α-epoxide</u> (XLVc) (1.8 g.), m.p. 67-68° (from

methanol), [α]$_D$- 49.5° (c. 0.6), ν $_{max.}$ 1,100 (OMe) cm.$^{-1}$,

τ 6.55-7.00 (m, 3-H), 6.77 (s, OMe), 7.21 (d, J (apparent)

<u>ca</u>. 2.5 Hz., 6-H), and 9.35 (s, 13β-Me) (Found: C, 80.78;

H, 11.89. C$_{29}$H$_{50}$O$_2$ requires C, 80.87; H, 11.7%).

<u>The α- and β-Epoxides</u> (XLVd) <u>and</u> (XLVe).- The epoxide (XLVa)

(5.2 g.) was heated under reflux with lithium aluminium hydride

(4.0 g.) in ether (600 ml.) for 1 hr.. The mixture was cooled

and the excess reducing agent removed by the addition of ethyl

acetate. Work up gave the diol (XLIXa) (3.4 g.) m.p.

148-149° (from methanol), [α]$_D$+ 13° (c. 1.08), ν $_{max.}$

(CHCl$_3$) 3620, 3440 (OH) cm.$^{-1}$, τ5.95 (m, W½ <u>ca</u>. 21 Hz.,

3-H), and 9.32 (s, 13β-Me). The diol (XLIXa) (1.0 g.) in

pyridine (25 ml.) at 10° was treated with methanesulphonyl

chloride (1.5 ml.). The mixture was allowed to stand for

2 hr. at room temperature and then poured into ice. The

mixture was extracted with ether and the ether extracts

washed with dilute hydrochloric acid and sodium bicarbonate

solution. Removal of the solvent gave the mesylate (XLIXb)

(1.2 g.), an oil, [α]$_D$+ 13° (c. 0.86), ν $_{max.}$ (thin film)

3540 (OH), and 1350, 1175 (S=O) cm.$^{-1}$, τ 5.00 (m, W½ <u>ca</u>.

26 Hz.,3-H), 7.05 (s, MeSO$_3$-), and 9.32 (s, 13β-Me).

The mesylate (XLIXb) (1.2 g.) was refluxed for 5 hr. in

a mixture of acetyl chloride (17 ml.), chloroform (17 ml.)

and diethylaniline (17 ml.). The mixture was poured into water and extracted with ether. The ether extract was washed with sodium bicarbonate solution, dried, and the solvent removed. The crude residue was chromatographed on deactivated alumina (70 g.) (eluting with petrol and 2% ether-petrol) and gave the 3α-acetoxy-olefin (XLVIIIc) (450 mg.), $\nu_{max.}$ 1740 (C=O), and 1245 (C-O) cm.$^{-1}$, τ 4.58 (m, $W\frac{1}{2}$ ca. 8 Hz., 6-H), 5.11 (m, $W\frac{1}{2}$ ca. 9 Hz., 3-H), 8.08 (s, OAc) and 9.29 (s, 13β-Me). The olefin (XLVIIIc) (450 mg.) was epoxidised using monoperphthalic acid for 48 hr. to give a mixture. Preparative t.l.c. [eluting (x 2) in benzene-ethyl acetate (19:1)] gave 3α-acetoxy-5,6α--epoxy-19-methyl-5α-cholestane (XLVd) (144 mg.), a gum, $[\alpha]_D$-36° (c. 1.1), $\nu_{max.}$ 1740 (C=O), and 1245 (C-O) cm.$^{-1}$, τ 5.14 (m, $W\frac{1}{2}$ ca. 8 Hz., 3-H), 7.40 (d, J ca. 3 Hz., 6-H), 8.04 (s, OAc), 9.39 (s, 13β-Me) (Found: C, 78.59; H, 10.88. $C_{30}H_{50}O_3$ requires C, 78.55; H, 10.99%), and 3α-acetoxy-5,6β-epoxy-19-methyl-5β-cholestane (XLVe) (168 mg.), m.p. 70-71° (from methanol), $[\alpha]_D$- 2° (c. 0.84), $\nu_{max.}$ 1740 (C=O), and 1240 (C-O) cm.$^{-1}$, τ 5.00 (m, $W\frac{1}{2}$ ca. 13 Hz., 3-H), 7.31 (m, $W\frac{1}{2}$ ca. 4 Hz., 6-H), 8.06 (s, OAc), and 9.32 (s, 13β-Me) (Found: C, 78.00; H, 11.08. $C_{30}H_{50}O_3$ C, 78.55; H, 10.99%).

5,6α-Epoxy-3α-hydroxy-19-methyl-5α-cholestane (XLVf).- The epoxide (XLVd) was hydrolysed and gave the hydroxy-α-epoxide (XLVf), m.p. 94-96° (from methanol), $[\alpha]_D$- 57° (c. 0.8), $\nu_{max.}$ 3570 (OH) cm.$^{-1}$, τ 6.04 (m, $W\frac{1}{2}$ ca. 8 Hz., 3-H), 7.00 (s, OH), 7.18 (d, J ca. 2.5 Hz., 6-H), and 9.35 (s, 13β-Me) (Found: C, 80.86; H, 11.94. $C_{28}H_{48}O_2$ requires C, 80.71; H, 11.61%).

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<u>5,6β-Epoxy-3α-hydroxy-19-methyl-5β-cholestane</u> (XLVg).-

The acetoxy-β-epoxide (XLVe) was hydrolysed and gave the

<u>hydroxy-β-epoxide</u> (XLVg), m.p. 130-131° (from methanol),

$[\alpha]_D$- 10.8°(c. 0.7), $\nu_{max.}$ 3640, 3430 (OH) cm.$^{-1}$,τ 5.91

(m, W$\frac{1}{2}$ ca. 11 Hz., 3-H), 7.20 (m, W$\frac{1}{2}$ ca. 4 Hz., 6-H), 7.54

(s, OH), and 9.32 (s, 13β-Me) (Found: C, 80.71; H, 11.45.

$C_{28}H_{48}O_2$ requires C, 80.71; H, 11.61%).

<u>3β-Acetoxy-5,6β-epoxy-19-methyl-5β-cholestane</u> (XLVh).-

The hydroxy-olefin (XLVIIIa) (2.5 g.) was stirred for 12 hr.

at room temperature with formic acid (25 ml.) and hydrogen

peroxide (3 ml. 100 vol.). The mixture was poured into water

and extracted with ether. The ether extract was washed with

sodium bicarbonate solution, dried and the solvent removed.

The crude product was heated under reflux for 30 min. in

methanolic potassium hydroxide (2.5%, 160 ml.). The usual

work up gave the crude triol (.Lb.) (2.3 g.). The triol

(. Lb..) was heated at 100° for 30 min. with toluene-p-sulphonic

acid (0.7g.) in acetic anhydride (35 ml.). The mixture was

cooled, poured into water and extracted with ether. The ether

extracts were washed with sodium bicarbonate solution, dried

and the solvent removed. This crude triacetate (Lc) was

heated under reflux for 15 min. in ethanol (113 ml.) containing

potassium hydroxide (3.42 g.). The usual work up gave a crude

product which was acetylated. Column chromatography of the

mixture (eluting with benzene) gave the pure <u>5,6β-epoxide</u> (XLVh)

(1.1 g.), a gum, $[\alpha]_D$ 0° (c. 0.71), $\nu_{max.}$ 1740 (C=O), and

1235 (C-O) cm.$^{-1}$, τ (CDCl$_3$) 5.20 (m, W$\frac{1}{2}$ ca. 22 Hz., 3-H), 7.14

(m, $W\frac{1}{2}$ ca. 4 Hz., 6-H), 8.02 (s, OAc), and 9.36 (s, 13β-Me)

(Found: C, 79.00; H, 11.11. $C_{30}H_{50}O_3$ requires C, 78.55;

H, 10.99%).

5,6β-Epoxy-3β-hydroxy-19-methyl-5β-cholestane (XLVi).-

The acetoxy-5,6β-epoxide (XLVh) was hydrolysed and gave

the hydroxy-5,6β-epoxide (XLVi), a gum, $[α]_D$+ 2.1°(c. 0.47),

$V_{max.}$ 3630 and ca. 3400 (OH) cm.$^{-1}$,τ6.32 (s, OH), 6.40

(m, $W\frac{1}{2}$ ca. 22 Hz., 3-H), 7.22 (m, $W\frac{1}{2}$ ca. 4 Hz., 6-H), and

9.33 (s, 13β-Me) (Found: C, 80.70; H, 11.48. $C_{28}H_{48}O_2$

requires C, 80.71; H, 11.61%).

Reaction of 3β-Acetoxy-5,6α-Epoxy-19-methyl-5α-cholestane (XLVb).-

The epoxide (XLVb) (1.5 g.) was reacted with boron trifluoride

for 1 min.. Preparative t.l.c. of the resultant mixture

[eluting with benzene-ethyl acetate (10:1)] gave three

fractions. The least polar was further chromatographed

[benzene-ethyl acetate (40:1)] to give 3β-acetoxy-5-formyl-19-

methyl-B-nor-5β-cholestane (LIIa) (196 mg.), a gum, $[α]_D$

+ 21° (c. 0.2), $V_{max.}$ 2720 (aldehyde C-H), 1740 (acetate

C=O), 1720 (aldehyde C=O), and 1235 (C-O) cm.$^{-1}$, τ 0.31

(s, CHO), 5.1 (m, $W\frac{1}{2}$ ca. 13 Hz., 3-H), 8.04 (s, OAc), and

9.33 (s, 13β-Me), mass spectrum: no molecular ion, first

significant peak possibly $^M-C_2H_4$-CHO, (m/e 401. 3422, $C_{27}H_{45}O_2$

requires 401. 3419), and 3β-acetoxy-6α,9-epoxy-19-methyl-

-1(10→ 5)-abeo-5α-cholestane (LIIIa) (45 mg.), m.p. 110-111°

(from methanol), $[α]_D$- 3.6° (c. 0.8), $V_{max.}$ 1740 (C=O),

and 1240 (C-O) cm.$^{-1}$,τ 5.0 (m, $W\frac{1}{2}$ ca. 13 Hz., 3-H),

6.33 (d, J $\underline{ca}$. 6 Hz., 6-H), 8.09 (s, OAc), and 9.40 (s,

13β-Me) (Found: C, 79.02; H, 11.00. $C_{30}H_{50}O_3$ requires

C, 78.55; H, 10.99%). The remaining two fractions were

acetylated. T.l.c. of the acetylated middle fraction [in

benzene-ethyl acetate (40:1)] gave 3β-acetoxy-6β-fluoro-

-5-hydroxy-19-methyl-5α-cholestane (LIV) (245 mg.), m.p.

143-144° (from acetone-methanol), $[\alpha]_D$- 21° (c. 0.7), $\vee$ max.

3608 and 3440 (OH), 1740 (C=O), and 1720 (C=O) cm.$^{-1}$,

τ 4.90 (m, W$\frac{1}{2}$ $\underline{ca}$. 20 Hz., 3-H), 5.86 (m, J_{HF} $\underline{ca}$. 49 Hz.,

6-H), 6.98 (s, OH), 8.03 (s, OAc) and 9.30 (s, 13β-Me)

(Found: C, 75.05; H, 10.89. $C_{40}H_{51}FO_3$ requires C, 75.28;

H, 10.74%), and 3β-acetoxy-19-methyl-5β-cholestan-6-one (LVa)

(275 mg.), m.p. 115-116° (from methanol), $[\alpha]_D$-29° (c. 0.7),

$\vee$ max. 1740 (acetate C=O), 1710 (C=O) and 1230 (C-O) cm.$^{-1}$,

τ 5.10 (m, W$\frac{1}{2}$ $\underline{ca}$. 8 Hz., 3-H), 8.00 (s, OAc), and 9.34 (s,

13β-Me) (Found: C, 78.38; H, 10.78. $C_{30}H_{50}O_3$ requires

C, 78.55; H, 10.99%), and 3β,6α-diacetoxy-5-ethyl-19-nor-

-5β-cholest-1(10)-ene (LVIa) (56 mg.), a gum, $[\alpha]_D$-23°

(c. 1.2), $\vee$ max. 1735 (C=O), and 1230 (C-O) cm.$^{-1}$, τ 4.73

(m, W$\frac{1}{2}$ $\underline{ca}$. 10 Hz., 1-H), 4.9-5.4 (m, 3,6-H), 7.98, and 8.03

(s, 2 x OAc), and 9.30 (s, 13β-Me). T.l.c. of the acetylated

most polar fraction [in benzene-ethyl acetate (10:1)] gave

3β,6α-diacetoxy-5-ethyl-19-nor-5β-cholest-9(10)-ene (LVIIa)

(224 mg.), a gum, $[\alpha]_D$+ 25° (c. 0.4), ε 5,300 at 215 n.m.,

$\vee$ max. 1735 (C=O), and 1235 (C-O) cm.$^{-1}$, τ 4.69-5.23 (m, 3,6-H),

8.00 (s, 2 x OAc), 9.20 (s, 13β-Me), and 9.30 (t, J $\underline{ca}$. 7 Hz.,

5β-Et) [Found: M (mass spectrum), 500.3848; C, 77.36; H,10.37.

$C_{32}H_{52}O_4$ requires M, 500.3865; C, 76.75; H, 10.47%¦and a second

fraction which was separated by t.l.c. on silver nitrate

impregnated silica (10%) [benzene-ethyl acetate (40:1)] to

give 3β,6α-diacetoxy-5-ethyl-14-methyl-18,19-bisnor-5β,

8α,9β,10α,14β-cholest-13(17)-ene (LVIIIa) (43 mg.), a gum,

$[\alpha]_D$+ 58° (c. 0.8), $\vee$ max. 1740 (C=O) and 1240 (C-O) cm.$^{-1}$,

τ 5.0 (m, W½ ca. 10 Hz., 3-H), 5.2 (m, W½ ca. 6 Hz., 6-H),

8.03,8.09 (s, 2 x OAc), 9.0 and 9.1 (shoulder) [d, C(21)

H₃], and 9.11 (s, 14β-Me) (double irradiation 88 Hz., downfield

caused the C(21)H₃‾doublet to collapse), M (mass spectrum)

500.3859 (9%) ($C_{32}H_{52}O_4$ requires 500.3865), and 3β,6α-diacetoxy-

19-methyl-1(10—→ 5)-abeo-5α-cholest-9 (10)-ene / (LIXa) (47 mg.), a gum,

$[\alpha]_D$+ 1.5° (c. 0.7), $\vee$ max. 1740 (C=O), and ca. 1235 (C-O) cm.$^{-1}$,

τ 4.9 (m, W½ ca. 22 Hz., 3-H), 5.2 (m, W½ ca. 20 Hz., 6-H),

8.00 and 8.05 (s, 2 x OAc), and 9.20 (s, 13β-Me), M (mass

spectrum) 500.3855 ($C_{32}H_{52}O_4$ requires 500.3865).

Treatment of the Fluorohydrin (LIV) with Base.- The fluorohydrin

(LIV) (150 mg.) was heated under reflux in methanolic potassium

hydroxide solution (5%) for 30 min. and poured into water.

Extraction with ether gave the hydroxy-epoxide (XLVa) (90 mg.),

identical with an authentic sample.

5-Ethyl-19-nor-5β-cholest-1(10)-en -3,6-dione (LVIb).-

The diacetate (LVIa) (50 mg.) was hydrolysed to give the diol

(LVIc) (38 mg.), an amorphous solid, $[\alpha]_D$- 5.5° (c. 0.8),

$\vee$ max. 3220 (OH) cm.$^{-1}$, τ 3.55 (s, 2 x OH, exchangeable

with D_2O), 4.56 (m, W½ ca. 12 Hz., 1-H), 5.98 (m, W½ ca.

14 Hz., 3-H), 6.57 (m, W½ ca. 7 Hz., 6-H), and 9.30

(s, 13β-Me), M (mass spectrum) 416.3653 ($C_{28}H_{48}O_2$ requires

416.3654). Oxidation of the diol (LVIc) gave the diketone

(LVIb) (30 mg.), a gum, $\vee_{max.}$ 1725 and 1715 (C=O) cm.$^{-1}$,

τ 4.56 (m, W½ ca. 8 Hz., 1-H), and 9.30 (s, 13β-Me).

Attempted Isomerisation of Diketone (LVIb).- The diketone

(LVIb) (10 mg.) was heated under reflux in ethanol (1 ml.)

with methanolic potassium hydroxide solution (30%, 0.15 ml.),

for 1 hr., The mixture was poured into water. Ether

extraction gave a crude, complex mixture which was not

investigated further.

The Diketones (LVIIb), (LVIIIb) and (LIXb).- The respective

diacetates were hydrolysed and oxidised to give the diketones.

The diacetate (LVIIa) (40 mg.) gave 5-ethyl-19-nor-5β-cholest-

9(10)e n -3,6-dione (LVIIb) (26 mg.), m.p. 101-102° (from

methanol), $[\alpha]_D$- 11° (c. 0.5), ε 5,600 at 215 n.m., $\vee_{max.}$

1725 (C=O) cm.$^{-1}$, τ 9.20 (s, 13β-Me), and 9.46 (t, J ca.

7 Hz., 5β-Et) [Found: M (mass spectrum), 412.3355; C, 81.31;

H, 10.93. $C_{28}H_{44}O_2$ requires M, 412.3341; C, 81.50; H, 10.75%].

The diacetate (LVIIIa) (40 mg.) gave 5-ethyl-14-methyl-18,19-bisnor-

-5β,8α,9β,10α,14β-cholest-13(17)en -3,6-dione (LVIIIb) (35 mg.),

a gum, $[\alpha]_D$+ 27°(c. 038), $\vee_{max.}$ 1720 (C=O) cm.$^{-1}$,τ 9.02

(s, 14β-Me and low-field branch C(21)H₃ doublet), 9.10 (s,

high-field branch C(21)H₃-doublet and side chain), 9.20 (side

chain), and 9.29 (t, J ca. 7 Hz., 5β-Et), M (mass spectrum)

412.3338 ($C_{28}H_{44}O_2$ requires 412.3341). The diacetate (LIXa)

(40 mg.) gave, after preparative t.l.c., 19-methyl-1(10→ 5)-

-abeo-5α-cholest-9(10)-en -3,6-dione (LIXb) (17 mg.), m.p. 102-104°

(from methanol), $[\alpha]_D$- 92° (c. 0.34), ν $_{max.}$ 1752 (3, C=O), and

1715 (6, C=O) cm.$^{-1}$, τ 9.21 (s, 13β-Me) (Found: C, 81.24;

H, 11.05. $C_{28}H_{44}O_2$ requires C, 81.50; H, 10.75%).

The δ -Lactone (LXI).- The aldehyde (LIIa) (75 mg.) in

acetone (6 ml.) at 0° was treated with Jones reagent [20]

(0.75 ml.) and set aside for 3 hr.. The mixture was poured

into water and extracted with ether to give a carboxylic

acid which was hydrolysed to give the hydroxy-carboxylic

acid (LXa), ν $_{max.}$ 3600,2500 (OH), and 1710 (C=O) cm.$^{-1}$.

A solution of the hydroxy-acid (LXa) was heated under reflux

for 15 min. in benzene containing a trace of toluene-p-sulphonic

acid, washed with sodium bicarbonate solution, dried and evaporated

to give 3α,5-methano-19-methyl-4-oxa-A-homo-B-nor-5α-cholestan-

4a-one (LXI) (60 mg.), m.p. 132-133° (from methanol), $[\alpha]_D$+

19° (c. 0.7), ν $_{max.}$ 1780 (C=O) cm.$^{-1}$, τ 5.5 (m, W$\frac{1}{2}$ ca. 8

Hz., 3-H), and 9.35 (s, 13β-Me) [Found:M(mass spectrum) 414.3495;

C, 81.48; H, 11.42. $C_{28}H_{46}O_2$ requires M, 414.3498; C, 81.10;

H, 11.18%].

The Hydroxy-Ester (LXb).- The δ -lactone (LXI) (35 mg.) was

heated under reflux for 6 hr. in methanolic potassium hydroxide

solution (10%). The mixture was poured into water, extracted

with ether, and the extract dried and evaporated. The crude

residue in ether at 0°C. was treated with an excess of diazomethane

for 15 min.. Acetic acid was added and the solvent removed

to give, after preparative t.l.c., the hydroxy-ester (LXb)

(14 mg.), a gum, ν $_{max.}$ 3450 (OH), and 1700 (C=O) cm.$^{-1}$,

τ 6.2-6.42 (m, 3-H), 6.29 (s,-COOMe), and 9.33 (s, 13β-Me).

The same ester was obtained directly from the hydroxy-acid

(LXa) using diazomethane in ether (as shown by t.l.c. and

^{1}H n.m.r. spectroscopy).

6α,9-Epoxy-3β-hydroxy-19-methyl-1(10→ 5)-abeo-5α-cholestane

(LIIIb).- The acetate (LIIIa) was hydrolysed to give the

alcohol (LIIIb), m.p. 56-58° and 104° (from methanol),

$[\alpha]_D$+ 5.5° (c. 0.75), $\nu_{max.}$ 3600 and 3430 (OH) cm.$^{-1}$, τ

(100 M.Hz., CDCl$_3$) 5.71 (m, W½ ca. 14 Hz., 3-H), 6.23 (d,

J ca. 6 Hz., 6-H), and 9.37 (s, 13β-Me) (Found: C, 80.84;

H, 11.62. C$_{28}$H$_{48}$O$_2$ requires C, 80.71; H, 11.61%).

6α,9-Epoxy-19-methyl-1(10→ 5)-abeo-5α-cholestan-3-one (LIIIc).-

The alcohol (LIIIb) (25 mg.) was oxidised to give the ketone

(LIIIc) (20 mg.), an amorphous solid, $[\alpha]_D$ 0° (c. 0.42),

$\nu_{max.}$ 1740 (C=O) cm.$^{-1}$, τ 6.10 (d, J ca. 6 Hz., 6-H) and

9.38 (s, 13β-Me), M (mass spectrum) 414.3501 (C$_{28}$H$_{46}$O requires

414.3498).

The Reaction of 3β-Acetoxy-6α,9-epoxy-19-methyl-1(10→ 5)-

abeo-5α-cholestane (LIIIa) with Boron Trifluoride in Acetic

Anhydride.- The ether (LIIIa) (62 mg.) as a solution in ether

(1.6 ml.) and acetic anhydride (2.6 ml.) at 0° was treated

with boron trifluoride etherate (0.36 ml.) for 2 hr.. The

mixture was poured into dilute sodium hydroxide solution (2N.),

ether extracted, washed with dilute hydrochloric acid (2N.) and

sodium bicarbonate solution, dried and the solvent removed to

give 3β,6α-diacetoxy-14,19-dimethyl-1(10→ 5)-abeo-18-nor-

5α,8α,9β,14β-cholest-13(17)-ene (LXVa) (68 mg.), a gum,

$[\alpha]_D^+$ 37° (c. 1.1), $\nu_{max.}$ 1740 (C=O) and 1245 (C-O) cm.$^{-1}$,

τ 5.00 (m, W$\frac{1}{2}$ ca. 15 Hz., 3-H), 5.34 (m, W$\frac{1}{2}$ ca. 7 Hz., 6-H),

8.00 and 8.05 (s, 2 x OAc), 8.98 and ca. 9.09 (C(21)H$_3$-

doublet), 9.12 and 9.21 (side chain methyls), and 9.18 (s,

14β-Me).

3β,6α-Dihydroxy-14,19-dimethyl-1(10→5)-abeo-18-nor-

5α,8α,9β,14β-cholest-13(17)-ene (LXVb).- Hydrolysis of the

diacetate (LXVa) gave the diol (LXVb), a gum, $[\alpha]_D^+$ 41°

(c. 0.9), $\nu_{max.}$ 3640 and ca. 3380 (OH) cm.$^{-1}$, τ 5.78

(m, W$\frac{1}{2}$ ca. 17 Hz., 3-H), 6.65 (m, W$\frac{1}{2}$ ca. 6 Hz., 6-H), 8.98

and ca. 9.10 (C(21)H$_3$-doublet), 9.10 and 9.20 (side chain

methyls), and 9.17 (s, 14β-Me), M (mass spectrum) 416.3657

($C_{28}H_{48}O_2$ requires 416.3654).

14,19-Dimethyl-1(10→5)-abeo-18-nor-5α,8α,9β,14β-cholest-

13(17)-en-3,6-dione (LXVc).- Oxidation of the diol (LXVb)

(62 mg.) gave the diketone (LXVc) (45 mg.), a gum, $[\alpha]_D^+$

91.5^o(c. 0.45), $\nu_{max.}$ 1750 and 1715 (3,6-C=O) cm.$^{-1}$,

τ 9.01 and 9.09 (C(21)H$_3$-doublet), 9.09 and 9.20 (side chain

methyls) and 9.12 (s, 14β-Me), M (mass spectrum) 412.3335

($C_{28}H_{44}O_2$ requires 412.3341).

3β,6α-Dihydroxy-14,19-dimethyl-1(10→5)-abeo-18-nor-13,17-

seco-5α,8α,9β,14β-cholestan-13,17-dione (LXVIIc).- The

diacetate (LXVa) (50 mg.) in ether (3 ml.) and pyridine

(2 ml.) was reacted with osmium tetroxide (100 mg.) for 3

days. The mixture was diluted with chloroform, saturated

with hydrogen sulphide, and passed through a short alumina

column. Removal of the solvent gave the diol (LXVI), a gum, $\nu_{max.}$ 3640, and ca. 3500 (OH), 1740 (C=O), and 1240 (C-O) cm.$^{-1}$, τ 4.97 (m, W$\frac{1}{2}$ ca. 14 Hz., 3-H), 5.33 (m, W$\frac{1}{2}$ ca. 6 Hz., 6-H), 7.98 and 8.06 (s, 2 x OAc), and 9.16 (s, 14β-Me), M (mass spectrum) 534. 3904 ($C_{32}H_{54}O_6$ requires 534.3920). The diol was treated with periodic acid (20 mg.) in ether (4 ml.) at room temperature for 2 hr.. The solution was diluted with ether and washed with sodium sulphite solution. Removal of the solvent and preparative t.l.c. [benzene-ethyl acetate (3:1)] gave the diketone (LXVIIa) (22 mg.), a gum, $\nu_{max.}$ 1745 (acetate C=O), 1718 (C=O) and 1240 (C-O) cm.$^{-1}$, τ 4.97 (m, W$\frac{1}{2}$ ca. 15 Hz., 3-H), 5.29 (m, W$\frac{1}{2}$ ca. 5 Hz., 6-H), 8.02 and 8.07 (s, 2x OAc), 8.94 and 9.05 (C(21)H$_3$-doublet), and 9.01 (s, 14β-Me). The diacetate (LXVIIa) in methanol (2.5 ml.) was stirred at room temperature for 45 min. with potassium carbonate (25 mg.) to give the monoacetate (LXVIIb) a gum, $\nu_{max.}$ 3640 and 3480 (OH), 1740 (acetate C=O), 1718 (C=O), and 1245 (C-O) cm.$^{-1}$, τ 5.31 (m, W$\frac{1}{2}$ ca. 6 Hz., 6-H), 5.75 (m, W$\frac{1}{2}$ ca. 12 Hz., 3-H), 8.00 (s, OAc), 8.92 and 9.03 (C(21)H$_3$-doublet), and 9.01 (s, 14β-Me). Extended treatment of the mono-acetate (LXVIIb) with potassium carbonate for 20 hr., as above, gave on work up and preparative t.l.c. [benzene-ethylacetate (1:1)] the diol (LXVIIc) (7 mg.), a gum, $\nu_{max.}$ 3640 and 3460 (OH), and 1710 (C=O) cm.$^{-1}$, τ 5.80 (m, W$\frac{1}{2}$ ca. 14 Hz., 3-H), 6.55 (m, W$\frac{1}{2}$ ca. 6 Hz., 6-H), 8.91 and 9.04 (C(21)H$_3$-doublet), 9.04 (s, 14β-Me)

and 9.10 and 9.19 (side chain methyls) (double irradiation

88 Hz. downfield caused the C(21)H$_3$-doublet to collapse to

a shoulder on the 14β-Me signal), M (mass spectrum) 448.3558

($C_{28}H_{48}O_2$ requires 448.3552).

The Reaction of the Ether (LIIIb) with Boron Trifluoride in

Acetic Anhydride and Acetic Acid.- The ether (LIIIb) (200 mg.)

in acetic acid (7 ml.) and acetic anhydride (1 ml.) was treated

with boron trifluoride etherate (1 ml.) for 2 hr. at 0°. The

reaction mixture was worked up as previously described.

Preparative t.l.c. [in benzene-ethyl acetate (40:1)] of

the mixture gave the $\triangle^{13,17}$-compound (LXVa) (93 mg.) and

the slightly impure $\triangle^{9,11}$-compound (LXVIIIa) (112 mg.),

a gum, ν $_{max.}$ 1740 (C=O) and 1240 (C-O) cm.$^{-1}$, τ 4.74 (m,

W$\frac{1}{2}$ ca. 6 Hz., 11-H), 4.85-5.25 (m, 3,6-H), 8.00 and 8.09 (s,

2 x OAc), and 9.38 (s, 13β-Me).

19-Methyl-1(10→ 5)-abeo-5α-cholest-9(11)-en -3,6-dione.

(LXVIIIc).- The diacetate (LXVIIIa) was hydrolysed and gave,

after preparative t.l.c., 3β,6α-dihydroxy-19-methyl-1(10→ 5)-

abeo-5α-cholest-9(11)-ene (LXVIIIb), m.p. 164-165° (from

methanol), [α]$_D$+ 29° (c. 0.9), ν $_{max.}$ 3640 and 3380 (OH)

cm.$^{-1}$, τ 4.79 (m, W$\frac{1}{2}$ ca. 7 Hz., 11-H), 6.1-6.7 (m, 3,6-H), and

9.38 (s, 13β-Me) (Found: C, 80.92; H, 12.05. $C_{28}H_{48}O_2$ requires

C, 80.71; H, 11.61%). The diol (LXVIIIb) (25 mg.) was oxidised

to the diketone (LXVIIIc) (23 mg.), m.p. 109-111° (from methanol),

[α]$_D$+ 35° (c. 0.46), ν $_{max.}$ 1755 (3 C=O) and 1715 (6 C=O) cm.$^{-1}$,

τ (100 M.Hz., CDCl$_3$) 4.44 (m, W$\frac{1}{2}$ ca. 8 Hz., 11-H), and 9.30

(s, 13β-Me) [Found: M (mass spectrum) 412.3345; C, 82.25;

H, 11.60. $C_{28}H_{44}O_2$ requires 412.3341; C, 81.50; H, 10.75%].

3β,6α-Diacetoxy-19-methyl-1(10 → 5)-abeo-5α-cholest-9(11)-en-12-

-one (LXIX).- The diacetate (LXVIIIa) (87 mg.) was dissolved

in dioxan (3 ml.) and water (0.6 ml.). Calcium carbonate

(40 mg.) and N-bromosuccinimide (110 mg.) were added. The

mixture was stirred and irradiated with a tungsten lamp

at room temperature for 1 hr.. The mixture was poured into

water, extracted with ether, and the ether extracts washed

with sodium bicarbonate solution.   Removal of the solvent

and preparative t.l.c. [benzene-ethyl acetate (19:1)] gave

the α,β-enone (LXIX) (30 mg.), a gum, $[\alpha]_D$ + 63.5° (c, 0.5),

$\lambda_{max.}$ 237 n.m., $\mathcal{E}$ 11,100, $\mathcal{V}_{max.}$ 1740 (acetate C=O), 1685

(12-C=O), and 1240 (C-O) cm.$^{-1}$, τ (100 M.Hz., $CDCl_3$) 4.35

(d, J ca. 2 Hz., 11-H), 4.80-5.12 (m, 3,6-H), 8.92 and 8.99

(s, 2 x OAc), and 9.18 (s, 13β-Me), M (mass spectrum) 514.3623

($C_{32}H_{50}O_5$ requires 514.3658).

Attempted Isomerisation of the Compounds (LIXb), (LXVIIIc) and

(LVIIa).- The olefin (LVIIa) remained unchanged when treated

with boron trifluoride in benzene for 24 hr. at room

temperature. The olefins (LIXb) and (LXVIIIc) remained

unchanged when treated with hydrogen bromide/acetic acid at

95° for 6 min. [22,70]

Reaction of 5,6α-Epoxy-3β-hydroxy-19-methyl-5α-cholestane

(XLVa).- The epoxide (XLVa) (2.0 g.) was reacted with boron

trifluoride for 2 min. . Preparative t.l.c. of the reaction

mixture [in benzene-ethyl acetate (3:1)] gave four fractions.

Two polar fractions were acetylated and further t.l.c. gave
the spiran (LIXa) (79 mg.), the Westphalen derivative
(LVIIa) (135 mg.), the ketone (LVa) (275 mg.) and the
$\triangle^{1,10}$-compound (LVIa) (100 mg.). The third fraction gave
the ether (LIIIb) (208 mg.). The fourth fraction (500 mg.)
was inseparable.

Reaction of 5,6α-Epoxy-3β-methoxy-19-methyl-5α-cholestane (XLVc).-
The epoxide (XLVc) (1.6 g.) was reacted with boron trifluoride
for 5 min.. Preparative t.l.c. of the reaction mixture [in
benzene-ethyl acetate (19:1)] gave four fractions. Two
polar fractions were acetylated and further t.l.c. [in benzene-
ethyl acetate (30:1)] gave 6α-acetoxy-3β-methoxy-19-methyl-1(10
→ 5)-abeo-5α-cholest-9(10)-ene (LIXc) (133 mg.), a gum,
$[\alpha]_D$+ 19° (c. 1.3), $\nu_{max.}$ 2825, 1095 (OMe), 1740 (C=O), and
1240 (C-O) cm.$^{-1}$, τ 5.34 (q, J (apparent) ca. 12 and 4 Hz.,
6-H), 6.30 (m, W½ ca. 10 Hz., 3-H), 6.83 (s, OMe), 8.06 (s,OAc),
and 9.23 (s, 13β-Me), M (mass spectrum) 472.3912 ($C_{31}H_{52}O_3$
requires 472.3916), 6α-acetoxy-3β-methoxy-5-ethyl-19-nor-
5β-cholest-9(10)-ene (LVIIc) (48 mg.), a gum, $[\alpha]_D$+ 40°
(c. 0.81), $\nu_{max.}$ 2825, 1090 (OMe), 1740 (C=O) and 1245 (C-O)
cm.$^{-1}$, τ 5.14 (q, J (apparent) ca. 12 and 4 Hz., 6-H), 6.53
(m, W½ ca. 10 Hz., 3-H), 6.77 (s, OMe), 8.05 (s, OAc), 9.22
(s, 13β-Me) and 9.37 (t, J ca. 7 Hz., 5β-Et), M (mass spectrum)
472.3899 ($C_{31}H_{52}O_3$ requires 472.3916), and 3β-methoxy-19-
methyl-5β-cholestan-6-one (LVb) (224 mg.), m.p. 94-94.5°
(from methanol), $[\alpha]_D$-44° (c. 0.66), $\nu_{max.}$ 2830, 1090
(OMe) and 1710 (C=O) cm.$^{-1}$, τ 6.62 (m, W½ ca. 8 Hz.,3-H),

6.79 (s, OMe), and 9.35 (s, 13β-Me) (Found: C, 80.86;

H, 11.72. $C_{29}H_{50}O_2$ requires C, 80.87; H, 11.71%). The

third fraction gave 6α,9-epoxy-3β-methoxy-19-methyl-1(10→5)-

-abeo-5α-cholestane (LIIId) (254 mg.), m.p. 87-88° (from

methanol), $[\alpha]_D$+ 4.6°(c. 0.72), $\nu_{max.}$ 2825, 1100 (OMe)

cm.$^{-1}$,τ 6.32 (d, J (apparent) ca. 6 Hz., 3,6-H), 6.77

(s, OMe), and 9.32 (s, 13β-Me) (Found: C, 81.03; H, 11.71.

$C_{29}H_{50}O_2$ requires C, 80.87; H, 11.71). The fourth fraction

(284 mg.) was inseparable.

Reaction of the Spiran (LIXc) with Boron Trifluoride in Acetic

Anhydride.- The spiro-compound (LIXc) (65 mg.) in acetic

anhydride (2.6 ml.) and ether (1.6 ml.) at 0° was treated

with boron trifluoride etherate (0.36 ml.) for 1 hr.. The

usual work up, followed by preparative t.l.c., gave the

diacetate (LIXa) (20 mg.). The diacetate (LIXa) was

hydrolysed and oxidised to give the diketone (LIXb). Both

compounds were identical in all respects to those previously

obtained.

The Ketone (LVIId).- The acetate (LVIIc) (20 mg.) was hydrolysed

and oxidised to give the ketone (LVIId) (10 mg.), a gum,

$[\alpha]_D$- 40° (c. 0.2), $\nu_{max.}$ 2830 (OMe), 1720 (C=O) cm.$^{-1}$,

τ6.4-ca. 6.75 (m, 3-H), 6.75 (s, OMe), 9.25 (s, 13β-Me), and

9.49 (t, J ca. 7 Hz., 5β-Et) (lit.,$^{(60a)}$ $[\alpha]_D$- 41°).

Reaction of the Ether (LIIId) with Boron Trifluoride in Acetic

Anhydride.- The ether (LIIId) (65 mg.) was reacted as above

for 12 hr.. Work up and preparative t.l.c. gave the diacetate

(LXVd) (15 mg.), a gum, τ 4.67-5.18 (m, 3,6-H), 7.98 and

107.

8.02 (s, 2 x OAc), 9.03 (d, J ca. 7 Hz., C(21)H₃), and 9.17

(s, 14β-Me). Hydrolysis of the diacetate (LXVd) gave the diol

(LXVe), a gum, τ 5.79 (m, W½ ca20 Hz., 3-H), 6.27 (m,

W½ ca. 8 Hz., 6-H), 9.00 (low-field branch C(21)H₃ doublet),

9.10 (high-field branch of C(21)H₃ doublet and side chain),

9.16 (s, 14β-Me), and 9.20 (side chain). Oxidation of the

diol gave the diketone (LXVc). This was identical in all

respects to the authentic sample.

Reaction of 3β-Acetoxy-5,6β-epoxy-19-methyl-5β-cholestane (XLVh).-

The epoxide (XLVh) (400 mg.) was reacted with boron trifluoride

for 5 min.. Preparative t.l.c. of the product mixture [eluting

(x 2) in benzene-ethyl acetate (19:1)] gave 3β-acetoxy-6β-

hydroxy-5-ethyl-14-methyl-18,19-bisnor-5β,8α,9β,10α,14β-

cholest-13(17)-ene (LVIIIc) (64 mg.), a gum, [α]$_D$+ 16° (c. 1.3),

ν$_{max.}$ 3640 and ca. 3500 (OH), 1740 (C=O), and 1245 (C-O)

cm.$^{-1}$, τ 4.97 (m, W½ ca. 8 Hz., 3-H), 6.75 (m, W½ ca. 24 Hz.,

6-H), 8.03 (s, OAc), 9.00 (lower branch C(21)H₃ doublet), 9.06

(s, 14β-Me), 9.09, shoulder and 9.10 (side chain and upper

branch C(21)H₃ doublet), and 9.20 (side chain) (double

irradiation 88 Hz. downfield caused the C(21)H₃ doublet to

collapse), M (mass spectrum) 458.3775 (C₃₀H₅₀O₃ requires

458.3760), 3β-acetoxy-19-methyl-5α-cholestan-6-one (LVc)

(20 mg.), m.p. 112° (from methanol), [α]$_D$- 6° (c. 0.4),

ν$_{max.}$ 1740 (acetate C=O), 1720 (C=O), and 1240 (C-O)

cm.$^{-1}$, τ ca. 5.0 (m, W½ ca. 18 Hz., 3-H), 8.06 (s, OAc), and

9.31 (s, 13β-Me) (Found: C, 78.86; H, 10.70. C₃₀H₅₀O₃

requires C, 78.55; H, 10.99%) and the aldehyde (LIIa) (135 mg.).

A further fraction (58 mg.) was an inseparable mixture.

The Diketone (LVIIIb).- The hydroxy-acetate (LVIIIc) (60 mg.) was hydrolysed and oxidised.   Preparative t.l.c. of the product gave the diketone (LVIIIb) (23 mg.) which was identical with that obtained previously.

The γ -Lactone (LXI). - The aldehyde (LIIa) (130 mg.) was oxidised and hydrolysed as described previously to give the hydroxy-acid (LXa). This was heated under reflux in benzene containing a trace of toluene-p-sulphonic acid to give the

γ -lactone (LXI) (105 mg.).   Both the aldehyde (LIIa) and the lactone (LXI) were identical with the authentic samples.

Reaction of 5,6β-Epoxy-3β-hydroxy-19-methyl-5β-cholestane

(XLVi).- The epoxide (XLVi) (400 mg.) was reacted with boron trifluoride for 5 min. to give a mixture, from which no identifiable products were isolated.

Reaction of 3α-Acetoxy-5,6α-epoxy-19-methyl-5α-cholestane

(XLVd).- The epoxide (XLVd) (600 mg.) was reacted with boron trifluoride for 5 min... Preparative t.l.c. of the resultant mixture [eluting (x2) in benzene-ethyl acetate (30:1)] gave 3α-acetoxy-6α-hydroxy-5-ethyl-19-nor-5β-cholest-9(10)-ene (LVIIe) (258 mg.), m.p. 131-132° (from methanol), $[\alpha]_D$ 0° (c. 0.74), ε 7,400 at 215 n.m., ν max. 3610 and 3460 (OH), 1730 (C=O), and 1245 (C-O) cm.$^{-1}$, τ 4.82 (m, W½ ca. 21 Hz., 3-H), 6.37 (m, W½ ca. 18 Hz., 6-H), 8.06 (s, OAc), 9.23 (s, 13β-Me) and 9.33 (t, J ca. 7 Hz., 5β-Et) (Found: C, 78.69; H, 10.89. $C_{30}H_{50}O_3$ requires C, 78.55; H, 10.99%),

3α-acetoxy-6α-hydroxy-5-ethyl-14-methyl-18,19-bisnor-5β,8α,9β,10α, 14β-cholest-13(17)-ene. (LVIIId) (126 mg.), a gum, $[\alpha]_D$ + 39.5° (c. 0.86), $\bigvee_{max.}$ 3400 (OH), 1730 (C=O), and 1245 (C-O) cm.$^{-1}$, τ 5.15 (m, broad, 3-H), 6.29 (m, W$\frac{1}{2}$ ca. 8 Hz., 6-H), 8.03 (s, OAc), 9.00-9.11 (C(21)H$_3$ doublet), 9.11-9.20 (side chain methyls), and 9.11 (14β-Me) (double irradiation 88 Hz., downfield caused the C(21)H$_3$ doublet to collapse), M (mass spectrum) 458.3764 ($C_{30}H_{50}O_3$ requires 458.3760),

3α-acetoxy-19-methyl-5β-cholestan-6-one (LVd) (168 mg.), m.p. 93-93.5° (from methanol), $[\alpha]_D$- 14.5° (c. 1.1), $\bigvee_{max.}$ 1740 (acetate C=O), 1710 (C=O), and 1235 (C-O) cm.$^{-1}$, τ 5.39 (m, W$\frac{1}{2}$ ca. 24 Hz., 3-H), 8.06 (s, OAc), and 9.35 (s, 13β-Me) (Found: C, 78.74; H, 10.82. $C_{30}H_{50}O_3$ requires C, 78.55; H, 10.99%) and 3α-acetoxy-5-formyl-19-methyl-B-nor-5β-cholestane (LIIb) (17 mg.), a gum, $\bigvee_{max.}$ 2700 (CHO), 1740 (acetate C=O), 1720 (aldehyde C=O), and 1240 (C-O) cm.$^{-1}$, τ 0.27 (s, CHO), 5.00 (m, W$\frac{1}{2}$ ca. 24 Hz., 3-H), 8.06 (s, OAc), and 9.33 (s, 13β-Me), M (mass spectrum) 458.3767 ($C_{30}H_{50}O_3$ requires 458.3760).

The Diketones (LVIIb) and (LVIIIb).- The hydroxy-acetates (LVIIe) and (LVIIId) were hydrolysed and oxidised. The compound (LVIIe) gave the diketone (LVIIb) and the compound (LVIIId) gave the diketone (LVIIIb). Both diketones were identical with their respective authentic samples.

The γ-Lactone (LXI).- The aldehyde (LIIb) (17 mg.) in acetone (2 ml.) at 0° was treated with Jones reagent[20]

(0.05 ml.) for 3 hr.. The mixture was poured into water. The
was
usual work up gave a crude product which/hydrolysed. This

latter product (LXc) was heated under reflux in benzene

containing a trace of toluene-p-sulphonic acid for 30 min..

The solution was washed with sodium bicarbonate solution,

dried and the solvent removed. Preparative t.l.c. of the

mixture [in benzene-ethyl acetate (10:1)] gave the δ -lactone

(LXI) (2.5 mg.), m.p. 127-129° (from methanol). This sample

was identical with an authentic sample of the δ -lactone

(LXI) (by t.l.c., i.r. spectrum, and mixed m.p. 127-129°).

Reaction of 5,6α-Epoxy-3α-hydroxy-19-methyl-5α-cholestane (XLVf).-

The epoxide (XLVf) (600 mg.) was reacted with boron trifluoride

for 2 min.. The crude reaction mixture was separated into

four fractions by preparative t.l.c. [in ether-petrol (9:11)].

These fractions were acetylated and further preparative t.l.c.

gave 3α,6α-diacetoxy-5-ethyl-19-nor-5β-cholest-9(10)-ene (LVIIf)

(63 mg.), a gum, $[\alpha]_D$+ 32°(c. 0.68), ε 6,750 at 215 n.m.,

$\nu_{max.}$ 1740 (C=O), and 1240 (C-O) cm.$^{-1}$, τ 4.60-5.23 (m, 3,6-H),

8.00 and 8.04 (s, 2 x OAc), 9.21 (s, 13β-Me) and 9.31 (t, J $\underline{ca.}$

7 Hz., 5β-Et) (Found: C, 76.25; H, 10.36. $C_{32}H_{52}O_4$ requires

C, 76.75; H, 10.47%), the ketone (LVd) (64 mg.), 3α-acetoxy-

-6α,9-epoxy-19-methyl-1(10$\longrightarrow$5)-abeo-5α-cholestane (LIIIe)

(70 mg.), a gum, $[\alpha]_D$+ 17° (c. 0.62), $\nu_{max.}$ 1740 (C=O),

and 1245 (C-O) cm.$^{-1}$, τ 5.01 (m, W½ $\underline{ca.}$ 17 Hz., 3-H), 6.18

(d, J (apparent) $\underline{ca.}$ 6 Hz., 6-H), 8.09 (s, OAc), and 9.40

(s, 13β-Me) (Found: C, 78.81; H, 10.70. $C_{30}H_{50}O_3$ requires

C, 78.55; H, 10.99%), and two further fractions. These

fractions were hydrolysed and oxidised and further t.l.c.

gave the diketone (LIXb) (30 mg.) and 3α,10-epoxy-5-ethyl-

-19-nor-5β,10α-cholestan-6-one (LXX) (26 mg.), a gum,

$[\alpha]_D$+ 21°(c. 0.5), $\vee$ max. 1720 (C=O) cm.$^{-1}$, τ 5.75 (m,

W½ ca. 14 Hz., 3-H), and 9.28 (s, 13β-Me), M (mass spectrum)

414.3494 ($C_{28}H_{46}O_2$ requires 414.3498).

The Ketones (LVIIb) and (LIIIc).-The acetoxy-compounds

(LVIIf) and (LIIIe) were hydrolysed and oxidised. The

compound (LVIIf) gave the diketone (LVIIb) which was

identical with the authentic sample. The compound (LIIIe)

gave the keto-ether (LIIIc), which was identical with the

authentic sample.

Treatment of the Ether (LXX) with Boron Trifluoride.- The

ether (LXX) (25 mg.) as a solution in benzene (5%) was

treated with boron trifluoride (ca. 0.05 ml.) for 30 min. at

room temperature. The usual work up gave a single product

which was oxidised to give the diketone (LVIIb) (25 mg.).

This sample was identical in all respects to the authentic

sample.

Reaction of 3α-Acetoxy-5,6β-epoxy-19-methyl-5β-cholestane

(XLVe).- The epoxide (XLVe) (320 mg.) was reacted with boron

trifluoride for 12 hr.. The resultant mixture was acetylated

and preparative t.l.c. [in benzene-ethyl acetate (10:1)]

gave 3α-acetoxy-19-methyl-5α-cholestan-6-one (LVe) (213 mg.),

a gum, $[\alpha]_D$-4° (c. 1.2), $\vee$ max. 1745 (acetate C=O), 1720 (C=O)
8 Hz.,
and 1240 (C-O) cm.$^{-1}$, τ 4.95 (m, W½ ca./3-H), 8.04 (s, OAc), and

9.30 (s, 13β-Me) (Found: C, 78.20; H, 10.84. $C_{30}H_{50}O_3$

requires C, 78.55; H, 10.99%) and 3α,5,6β-triacetoxy-19-methyl-

-5α-cholestane (LXXIV) (40 mg.), a gum, $[\alpha]_D$- 45.5°(c. 0.8),

$\nu_{max.}$ 1750 (C=O), and ca. 1240 (C-O) cm.$^{-1}$, τ 4.34 (m, W½ ca.

5 Hz., 6-H), 4.90 (m, W½ ca. 10 Hz., 3-H), 8.01 (s, 2 x OAc),

8.09 (s, OAc), and 9.29 (s, 13β-Me); mass spectrum: no

molecular ion, the first significant peak possibly [M-2 moles

HOAc] 440.3676 ($C_{30}H_{48}O_2$ requires 440.3654).

Reaction of 5,6β-Epoxy-3α-hydroxy-19-methyl-5β-cholestane

(XLVg).- The epoxide (XLVg) (330 mg.) was treated with

boron trifluoride for 2 min.. The resultant mixture could

not be separated.

5,6α-Epoxy-3β-hydroxy-19-methylene-5α-cholestane (LXXXIVa).-

The diene (XLVII) [60a] (2.2 g.) was epoxidised to give the

hydroxy-epoxide (LXXXIVa) (2.35 g.), a gum, $[\alpha]_D$- 55°

(c. 0.8), $\nu_{max.}$ 3630 and 3380 (OH) and 3090, 1640, and 920

(CH_2=CHR) cm.$^{-1}$, τ 4.1-5.2 (m, -CH=CH_2), 6.35 (m, W½ ca. 25 Hz.,

3-H), 6.82 (s, OH), 7.12 (d, J (apparent) ca. 3.5 Hz., 6-H),

and 9.49 (s, 13β-Me) (Found: C, 81.21; H, 10.96. $C_{28}H_{46}O_2$

requires C, 81.10; H, 11.18%).

3β-Acetoxy-5,6α-epoxy-19-methylene-5α-cholestane (LXXXIVb)[74].-

Acetylation of the hydroxy-epoxide (LXXXIVa) (2.35 g.) gave

the acetoxy-epoxide (LXXXIVb) (2.1 g.), m.p. 75-76° (from

methanol), $[\alpha]_D$- 55° (c. 0.83), τ 4.00-5.60 (m,-CH=CH_2

and 3-H), 7.11 (d, J (apparent) ca. 4 Hz., 6-H), 8.10

(s, OAc), and 9.48 (s, 13β-Me) (lit.[74] m.p. 77°, $[\alpha]_D$-53°).

<u>5,6α-Epoxy-3β-methoxy-19-methylene-5α-cholestane</u> (LXXXIVc).-

The hydroxy-diene (XLVII)[(60a)] (1.1 g.) as a solution in

trimethylorthoformate (11 ml.) was treated with perchloric

acid (1.1 ml. 60% w/v.) at room temperature for 15 min..

The mixture was poured into sodium bicarbonate solution and

extracted with ether. The ether extract was dried and the

solvent removed. The crude product was epoxidised to give

the <u>α-epoxide</u> (LXXXIVc) (1.15 g.), m.p. 87-88° (from methanol),

$[α]_D$- 63.5°(c. 0.77), $\vee_{max.}$ 2830 (OMe), 3090 and 920

(CH_2= CHR) cm.$^{-1}$,Υ 4.04-5.20 (m, -CH=CH_2), 6.69 (m, W½ <u>ca.</u>

21 Hz., 3-H), 6.81 (s, OMe), 7.14 (d, J (apparent) <u>ca.</u> 4 Hz.,

6-H) and 9.49 (s, 13β-Me) (Found: C, 81.37; H, 11.38.

$C_{29}H_{48}O_2$ requires C, 81.25; H, 11.29%).

<u>Reaction of 3β-Acetoxy-5,6α-epoxy-19-methylene-5α-cholestane</u>

(LXXXIVb).- The epoxide (LXXXIVb) (2 g.) was treated with

boron trifluoride for 5 min.. Preparative t.l.c. of the

resultant mixture [in benzene-ethyl acetate (25:1)] gave the

<u>dimeric ether</u> (LXXXVI) (430 mg.), m.p. 171-173° (from

methanol), $[α]_D$+ 10.5°(c. 2.1), $\vee_{max.}$ 3610, 3450 (OH),

1740, 1720 (C=O), 1245 (C-O) and 3080 and 915 (CH_2=CHR) cm.$^{-1}$,

Υ(100 M.Hz., $CDCl_3$)   2.8-4.1 (m, (x 2) RCH=CR_2), 4.5-5.4

(m, (x 2) R_2C = CH_2 and (x 2)-CHOCOR), 6.70 (m, W½ <u>ca.</u> 13 Hz.,

(x 2) -CHOR), 8.00 (s, OAc), 8.09 (s, OAc), 9.02 and 9.09

(C(21)H_3 doublet) 9.10/9.12 and 9.18/9.20 [(x 2) side chain

doublets], 9.18 (s, 14β-Me), and 9.46 (s, 13β-Me) (double

irradiation 147 Hz. downfield caused the C(21)H_3 doublet

to collapse [Found: M.W. 882 (osmometry) C, 78.29; H, 10.74.

$C_{60}H_{96}O_6$ requires M.W. 912; C, 78.89; H, 10.59%], and a

second fraction. Further t.l.c. of this fraction [eluting

(x 2) in benzene-ethyl acetate (40:1)] gave 3β-acetoxy-6β-

-fluoro-5-hydroxy-19-methylene-5α-cholestane (LXXXVIIa)

(780 mg.), m.p. 163° (from methanol), $[\alpha]_D$+ 15.5°(c. 0.75),

$\nu_{max.}$ 3610, 3450 (OH), 1740, 1720 (acetate C=O), ca. 1250

(C-O) and 3090 and 920 (CH_2=CHR) cm.$^{-1}$, τ 3.35-4.00 (m, X

part of ABX, CH_2=CHR), 4.40-5.4 (m, 3-H and A B part of ABX,

CH_2=CHR), 5.70 (m, J_{HF}ca. 48 Hz., 6-H), 6.60 (s, OH), 8.02

(s, OAc), and 9.41 (s, 13β-Me) (Found: C, 76.02; H, 10.62.

$C_{30}H_{49}FO_3$ requires C, 76.50; H, 10.36%), and the epoxide

(LXXXIVb) (360 mg.).

Treatment of the Fluorohydrin (LXXXVIIa) with Base.- The

fluorohydrin (LXXXVIIa) was heated under reflux for 30 min.

in methanolic potassium hydroxide (5%). The mixture was

cooled and poured into water. Ether extraction gave the

hydroxy-epoxide (LXXXIVa), identical with an authentic·sample.

Reaction of 5,6α-Epoxy-3β-hydroxy-19-methylene-5α-cholestane

(LXXXIVa).- The epoxide (LXXXIVa) (1.0 g.) was reacted with

boron trifluoride for 5 min.. The reaction mixture was

acetylated. Preparative t.l.c. [eluting (x 4) in benzene-

ethyl acetate (25:1)] gave the fluorohydrin (LXXXVIIa) (330 mg.).

No other identifiable products were isolated.

Reaction of 5,6α-Epoxy-3β-methoxy-19-methylene-5α-cholestane

(LXXXIVc).- The epoxide (LXXXIVc) (760 mg.) was treated with

boron trifluoride for 2 min.. Preparative t.l.c. [in benzene-ethyl acetate (19:1)] gave five fractions. A fraction of highly polar material (230 mg.) was found to be inseparable. A second fraction was acetylated and further t.l.c. gave 6α-acetoxy-3β-methoxy-5-ethenyl -19-nor-5β-cholest-9(10)-ene (XCa) (91 mg.), a gum, $[\alpha]_D + 66°$ (c. 0.52), $\nu_{max.}$ 3070, 1635 and 910 (CH_2=CHR-), 2820 (OMe), 1740 (C=O), and 1245 (C-O) cm.$^{-1}$, τ 3.8-4.32 (m, X part of ABX system, CH_2=CH-), 4.8-5.50 (m, A B part of ABX system, CH_2=CH- and 6-H), 6.57 (m, $W\frac{1}{2}$ ca. 10 Hz., 3-H), 6.80 (s, OMe), 8.06 (s, OAc), and 9.21 (s, 13β-Me), M (mass spectrum) 470.3770 ($C_{31}H_{50}O_3$ requires 470.3760). Preparative t.l.c. of a further two fractions gave 6β-fluoro-5-hydroxy-3β-methoxy-19-methylene-5α--cholestane (LXXXVIIb) (114 mg.), m.p., 147-148° (from methanol), $[\alpha]_D + 34°$ (c. 2.0), $\nu_{max.}$ 3630, 3450 (OH), 3090, 1637 and 940 (CH_2=CH-) 2835 (OMe) cm.$^{-1}$, τ 3.31-3.96 (m, X part of ABX system, CH_2=CH-), 4.46-5.30 (m, A B part of ABX system, CH_2=CH-), 5.60 (m, J_{HF}. ca. 50 Hz., 6-H), 6.34 (m, $W\frac{1}{2}$ ca. 24 Hz., 3-H), 6.66 (s, OMe), and 9.42 (s, 13β-Me) (Found: C, 77.70; H, 10.98. $C_{29}H_{49}FO_2$ requires C, 77.62; H, 11.01%), 6α-hydroxy-3β-methoxy-5-ethenyl-14--methyl-18,19-bisnor-5β,8α,9β,10α,14β-cholest-13(17)-ene (LXXXVIII) (15 mg.), a gum, $\nu_{max.}$ 3630 (OH), 3080, 1635, and 930 (CH_2=CH-), 2835 (OMe) cm.$^{-1}$, τ 3.60-4.05 (m, X part of the ABX system CH_2=CH-), 4.77-5.32 (m, AB part of the ABX system, CH_2=CH-), 6.25 (m, $W\frac{1}{2}$ ca. 8 Hz., 6-H),

6.61(m,W$\frac{1}{2}$ $\underline{ca}$. 9 Hz., 3-H), 6.94 (s, OMe), 9.01 and 9.11 (C(21)H$\frac{-}{3}$

doublet), 9.11 and 9.19 (side chain methyls), and 9.19 (s,

14β-Me) (double irradiation 88 Hz., downfield caused the

C(21)H$\frac{-}{3}$ doublet to collapse), M (mass spectrum) 428.3648

($C_{29}H_{48}O_2$ requires 428.3654), 3β-methoxy-19-methylene-5β-

-cholestan-6-one (LXXXIX) (107 mg.), a gum, $[\alpha]_D$-37°(c. 1.7),

$\vee$ max. 3100, 1640 and 925 (CH$_2$=CH-), 2835 (OMe) and 1713 (C=O)

cm.$^{-1}$, τ 3.86-4.42 (m, X part of ABX system, CH$_2$=CH-), 4.73-

5.27 (m, A B part of ABX system, CH$_2$=CH-), 6.58 (m, W$\frac{1}{2}$

$\underline{ca}$. 7 Hz., 3-H), 6.77 (s, OMe), and 9.39 (s, 13β-Me)

(Found: C, 81.18; H, 11.00. $C_{29}H_{48}O_2$ requires C, 81.25;

H, 11.29%), and the epoxide (LXXXIVc) (42 mg.). The fifth

non-polar fraction (53 mg.) was not investigated any further.

3β-Methoxy-5-ethenyl-19-nor-5β-cholest-9(10)-en-6-one (XCb).-

The acetate (XCa) (27 mg.) was hydrolysed and oxidised and

gave, after t.l.c., the ketone (XCb) (10 mg.), m.p. 69-71°

(from methanol), $\vee$ max. 2830 (OMe), 1718 (C=O), and 935

(CH$_2$=CH-) cm.$^{-1}$, τ (100 M.Hz., CDCl$_3$) 4.00-4.29 (m, X part

of ABX system, CH$_2$=CH-), 4.84-5.16 (m, A B part of ABX system,

CH$_2$=CH-), 6.50 (m, W$\frac{1}{2}$ $\underline{ca}$. 8.5 Hz., 3-H), 6.71 (s, OMe),

and 9.22 (s, 13β-Me), M (mass spectrum) 426.3502 ($C_{29}H_{46}O_2$

requires 426.3498).

Reaction of 3β-Acetoxy-5,6α-epoxy-5α-cholestane (XIVd).[13] -

The epoxide (XIVd) (516 mg.) was reacted with boron trifluoride

for 5 min.. Preparative t.l.c. [in benzene-ethyl-acetate

(10:1)] gave the fluorohydrin (XVb)[1b] (221 mg.). The

remaining material was not investigated any further..

The α- and β-Epoxides (CXIIIa) and (CXIIIb).- 6β-Acetoxy-3β-
-methoxy-5-methyl-19-nor-5β-cholest-9(10)-ene[28] (8.4 g.)

was epoxidised to give a mixture of two compounds. Repeated

preparative t.l.c. of this mixture (in chloroform) gave

6β-acetoxy-9,10-epoxy-3β-methoxy-5-methyl-19-nor-5β-10α-

-cholestane (CXIIIa) (4.3 g.), m.p. 86-87° (from methanol),

$[\alpha]_D$+ 10.5° (c. 1.2), ν max. $(CHCl_3)$ 2830 (OMe), 1735 (C=O)

and ca. 1240 (C-O) cm.$^{-1}$, τ $(CDCl_3)$ 4.99 (t, J (apparent)

ca. 9 Hz., 6-H), 6.41 (m, W½ ca. 8 Hz., 3-H), 6.69 (s, OMe),

8.01 (s, OAc), 8.78 (s, 5β-Me), and 9.24 (s, 13β-Me) (Found:

C, 76.22; H, 10.95. $C_{30}H_{50}O_4$ requires C, 75.90; H, 10.62%),

and 6β-acetoxy-9,10-epoxy-3β-methoxy-5-methyl-19-nor-5β-9β-

-cholestane (CXIIIb) (2.85 g.), a gum, $[\alpha]_D$+ 63° (c. 1.1),

ν max. $(CHCl_3)$ 1725 (C=O), and 1250 (C-O) cm.$^{-1}$, τ $(CDCl_3)$

5.15 (q, J (apparent) ca. 12 and 4 Hz., 6-H), 6.41 (t, J

(apparent) ca. 6 Hz., 3-H), 6.69 (s, OMe), 7.98 (s, OAc),

8.84 (s, 5β-Me), and 9.19 (s, 13β-Me) (Found: C, 76.10;

H, 10.28. $C_{30}H_{50}O_4$ requires C, 75.90; H, 10.62%).

9,10-Epoxy-6β-hydroxy-3β-methoxy-5-methyl-19-nor-5β,10α-

-cholestane (CXIIIc).- The acetoxy-epoxide (CXIIIa) (100 mg.)

was hydrolysed and gave the hydroxy-α-epoxide (CXIIIb) (89 mg.),

m.p. 134-135° (from aqueous methanol), $[\alpha]_D$+ 25° (c. 0.8),

ν max. $(CHCl_3)$ 3610, 3640 (OH), and 1090 (OMe) cm.$^{-1}$,

τ $(CDCl_3)$ 6.00-6.60 (m, 3,6-H), 6.71 (s, OMe), 8.89 (s,

5β-Me), and 9.27 (s, 13β-Me) (Found, 77.82; H, 11.05.

$C_{28}H_{48}O_3$ requires C, 77.72; H, 11.18%).

<u>9,10-Epoxy-3β-methoxy-5-methyl-19-nor-5β,10α-cholestan-6-one</u>

(CXIIId).[88] - The hydroxy-epoxide (CXIIIc) (89 mg.) was

oxidised and gave the keto-epoxide (CXIIId) (72 mg.), m.p.

94-96° (from aqueous methanol-acetone), $[\alpha]_D$- 8.4°(c. 1.1),

$\nu_{max.}$ (CHCl$_3$) 1712 (C=O) cm.$^{-1}$, τ 6.46 (m, W$\frac{1}{2}$ ca. 8 Hz.,

3-H), 6.75 (s, OMe), 8.79 (s, 5β-Me), and 9.24 (s, 13β-Me)

(lit.,[88a] m.p. 97°, $[\alpha]_D$ - 6.5°).

<u>The β-Epoxides</u> (CXIIIe) <u>and</u> (CXIIIf).- The acetoxy-epoxide

(CXIIIb) (1.10 g.) was hydrolysed and gave <u>9,10-epoxy-6β-</u>

<u>hydroxy-3β-methoxy-5-methyl-19-nor-5β,9β-cholestane</u> (CXIIIe)

(950 mg.), a gum, $[\alpha]_D$+ 46.5°(c. 1.1), $\nu_{max.}$ (CHCl$_3$) 3480

(OH) cm.$^{-1}$, τ (CDCl$_3$) 6.3-7.0 (m, 3,6-H), 6.71 (s, OMe),

8.81 (s, 5β-Me), and 9.20 (s, 13β-Me) (Found: C, 77.56;

H, 11.52. C$_{28}$H$_{48}$O$_3$ requires C, 77.72; H, 11.18%). Oxidation

of the hydroxy-epoxide (CXIIIe) (900 mg.) gave <u>9,10-epoxy-</u>

<u>3β-methoxy-5-methyl-19-nor-5β,9β-cholestan-6-one</u> (CXIIIf)

(800 mg.), a gum, $[\alpha]_D$+ 82° (c. 1.4), $\nu_{max.}$ (CHCl$_3$) 1715 cm.$^{-1}$,

τ 6.46 (m, W$\frac{1}{2}$ ca. 8 Hz., 3-H), 6.70 (s, OMe), 8.65 (s, 5β-Me),

and 9.19 (s, 13β-Me) (Found: C, 78.19; H, 10.98.

C$_{28}$H$_{46}$O$_3$ requires C, 78.09; H, 10.77%).

<u>3β-Methoxy-5-methyl-19-nor-5β-cholest-9(10)-ene</u> (CXIVc).[28] -

3β-Methoxy-5-methyl-19-nor-5β-cholest-9(10)en-6-one (CXIVb)[28]

(271 mg.) and freshly recrystallised benzenesulphonylhydrazine

(150 mg.) were heated under reflux in ethanol (5 ml.)

containing concentrated hydrochloric acid (1 drop) for 20

min.. The mixture was cooled, poured into dilute hydrochloric

acid and extracted with ether. The ether extracts were washed

with sodium bicarbonate solution, dried and the solvent

removed to give the   benzenesulphonylhydrazone   (CXIVd)

(293 mg.), m.p. 153-155° (from methanol), $[\alpha]_D$+ 11.5° (c.

0.65), ν max. 3230, 3080, 2830, 1350, 1220, 1175, 1095,

865, and 690 cm.$^{-1}$, τ 1.50-2.70 (m, aromatic, 5 x C-H)

6.43-6.85 (m, 3-H), 6.81 (s, OMe), 8.80 (s, 5β-Me), and

9.30 (s, 13β-Me) (Found: C, 71.32; H, 9.27; N, 5.00.

$C_{33}H_{52}N_2O_3S$ requires C, 71.19; H, 9.42; N, 5.03%). The

hydrazone (CXIVd) (80 mg.) and sodium borohydride (200

mg.) were heated under reflux for 8 hr. in dry, peroxide

free, dioxan. The mixture was poured into water. Ether

extraction gave, after preparative t.l.c., the C(6)-desoxy-

compound (CXIVc) (65 mg.), m.p. 58-59° (from ethanol), $[\alpha]_D$+

62° (c, 1.05), τ 6.60 (m, W½ ca. 9 Hz., 3-H), 6.76 (s, OMe),

8.85 (s, 5β-Me), and 9.22 (s, 13β-Me) (lit.,[28] m.p. 60°,

$[\alpha]_D$+ 61.6).

The α- and β-Epoxides (CXIIIg) and (CXIIIh).- The olefin (CXIVc)

(525 mg.) was epoxidised, and preparative t.l.c. of the

resultant mixture [eluting (x 2) in chloroform-petrol

(3:2)] gave 9,10-epoxy-3β-methoxy-5-methyl-19-nor-5β,10α-

-cholestane (CXIIIg) (245 mg.), a gum, $[\alpha]_D$+ 29.5° (c. 0.78),

τ 6.55 (m, W½ ca. 10 Hz., 3-H), 6.78 (s, OMe), 8.85

(s, 5β-Me), and 9.29 (s, 13β-Me) (Found: C, 80.66; H, 11.59.

$C_{28}H_{48}O_2$ requires C, 80.71; H, 11.61%), and 9,10-epoxy-3β-

methoxy-5-methyl-19-nor-5β,9β-cholestane (CXIIIh) (160 mg.),

a gum, $[\alpha]_D$+ 55.5°(c. 0.48), τ 6.55 (m, W½ ca. 10 Hz., 3-H),

6.85 (s, OMe), 8.90 (s, 5β-Me), and 9.18 (s, 13β-Me) (Found:

C, 80.94; H, 11.15. $C_{28}H_{48}O_2$ requires C, 80.71; H,

11.61%).

Reaction of the Keto-α-epoxide (CXIIId).- The epoxide (CXIIId)[88]
(600 mg.) was reacted with boron trifluoride for 7

min.. Preparative t.l.c. on silver nitrate impregnated silica

(10%) [in benzene-ethyl acetate (19:1)] gave the diene

(CXVa) (144 mg.), $[\alpha]_D$- 105° (c. 1.31), λ max. 247 n.m.,

$\mathcal{E}$ max. 29,000,τ 3.78 (s, 11,12-H), 6.58 (m, W$\frac{1}{2}$ ca. 9 Hz.,

3-H), 6.73 (s, OMe), 8.71 (s, 5β-Me), and 9.23 (s, 13β-Me)

(lit.,[88a] m.p. 70°, $[\alpha]_D$- 105°, λ max. 248 n.m., $\mathcal{E}$ max.

29,000), the diene (CXVIa) (146 mg.), m.p. 84-85° (from

methanol), $[\alpha]_D$- 196° (c. 1.02), λ max. 243 n.m., $\mathcal{E}$ max.

9,200,τ 4.18 (m, 1,11-H), 6.75 (s, OMe), ca. 6.95

(m, broad, 3-H), 8.81 (s, 5β-Me), and 9.26 (s, 13β-Me) (lit.,

[88a] m.p. 85-86°, $[\alpha]_D$- 200°, λ max. 242 n.m., $\mathcal{E}$ max.

9,200), 3β-methoxy-5,14-dimethyl-18,19-bisnor-5β-8α,9β,14β-

-cholesta-1(10),13(17)-dien -6-one (CXVIIa) (118 mg.), a gum,

$[\alpha]_D$+ 129° (c. 1.26), ν max. (thin film) 1715 (C=O) cm.$^{-1}$,

τ (100 M.Hz., CDCl$_3$) 4.66 (m, W$\frac{1}{2}$ ca. 12 Hz., 1-H),

6.64 (s, OMe), 6.76 (m, W$\frac{1}{2}$ ca. 24 Hz., 3-H), 8.64 (s, 5β-Me),

8.99 (s, 14β-Me), and 9.07 (d, J ca. 7 Hz., C(21)H$_3$),

τ (60 M.Hz., C$_6$D$_6$), 8.84 (s, 5β-Me), 8.94 and 9.05

(C(21)H$_3$-doublet), 9.05 and 9.15 (side chain methyls), and

9.15 (s, 14β-Me) (double irradiation 88 Hz. downfield caused

the C(21)H$_3$ doublet to collapse) (Found: C, 80.99; H, 10.91.

$C_{28}H_{44}O_2$ requires C, 81.50; H, 10.75%), and the hydroxy-backbone -

compound (CXVIIIa) (29 mg.), an amorphous solid, ν max.

(CHCl$_3$) 3620, 3500 (OH), and 1710 (C=O) cm.$^{-1}$, τ (CDCl$_3$)

6.46 (m, W$\frac{1}{2}$ ca. 9 Hz., 3-H), 6.74 (s, OMe), 8.60 (s, 5β-Me),

9.00 and 9.11 (C(21)H$_3$ doublet), 9.00 (14β-Me), and

9.11 and 9.21 (side chain methyls), τ (C$_6$D$_6$) 8.92 and 9.03

(C(21)H$_3$), 9.03 and 9.14 (side chain methyls), 9.05 (s,

5β-Me), and 9.14 (s, 14β-Me).

Hydrogenation of the Compound (CXVIIa).- The diene (CXVIIa)

(43 mg.) as a solution in ethyl acetate (10 ml.) was

stirred under an atmosphere of hydrogen with a palladium -

charcoal catalyst for 3 hr..   The mixture was filtered and

the solvent removed to give a mixture of isomers (37 mg.)

which were inseparable by t.l.c., τ (CDCl$_3$) 6.66 (methoxyl-

methyls), 6.73 (m, W$\frac{1}{2}$ ca. 22 Hz., 3-H's), ca. 8.73 (5β-methyls),

and ca. 9.03 (14β-methyls).

Reaction of the Keto-β-epoxide (CXIIIf).- The epoxide (CXIIIf)

(560 mg.) was reacted with boron trifluoride for 7 min..

Preparative t.l.c. of the resultant mixture on silver nitrate

impregnated silica (10%) [eluting with benzene-ethyl acetate

(19:1)] gave the diene (CXVIa)[88a] (147 mg.), the backbone -

compound (CXVIIa) (29 mg.), the diene (CXVa)[88a] (128 mg.),

m.p. 68-69° (from methanol), the diketone (CXIXa) (30 mg.),

a gum, ν max. 2830, 1100 (OMe), 1730 (6-C=O), and 1700 (C=O)

cm.$^{-1}$, τ (CDCl$_3$) 6.76 (s, OMe), ca. 6.76 (m,3,H), 8.79

(s, 5β-Me), and 9.32 (s, 13β-Me), M (mass spectrum) 430.3442

(C$_{28}$H$_{46}$O$_3$ requires 430.3448), and the hydroxy-backbone -

compound (CXVIIIb) (38 mg.), a gum, $\nu_{max.}$ (thin film)
3500 (OH), 1710 (C=O), and 1105 (OMe) cm.$^{-1}$, τ (CDCl$_3$)
6.64 (s, OMe), 6.32-6.89 (m, 3-H), 8.80 (s, 5β-Me), 9.00
and 9.12 (C(21)H$_3$), 9.02 (s, 14β-Me) and 9.12 and 9.22 (side
chain methyls) [double irradiation 88 Hz. downfield (in C$_6$D$_6$)
caused the C(21)H$_3$ doublet to collapse]. ·

Dehydration of the Alcohol (CXVIIIb).- The hydroxy-olefin
(CXVIIIb) in pyridine was treated with thionyl chloride at
0° for 5 min..[21] The mixture was poured into crushed ice.
Ether extraction gave the diene (CXVIIa), identical with an
authentic sample by t.l.c..

Reaction of the Acetoxy-α-epoxide (CXIIIa).- The epoxide
(CXIIIa) (700 mg.) was treated with boron trifluoride for
7 min.. Preparative t.l.c. of the resultant mixture (in
chloroform)gave 6β-acetoxy-3β-methoxy-5,14-dimethyl-18,19-bisnor-
5β,8α,9β,14β-cholesta-1(10), 13(17)-diene (CXVIIb) (390 mg.),a gum,
[α]$_D$+ 67° (c. 0.52), $\nu_{max.}$ (CHCl$_3$) 1730 (C=O), 1250 (C-O),
and 1095 (OMe) cm.$^{-1}$, τ(CDCl$_3$) 4.68 (m, W½ ca. 10 Hz.,
1-H), 5.18 (t, J (apparent) ca. 9 Hz., 6-H), 6.32-6.72 (m,
3-H), 6.71 (s, OMe), 7.94 (s, OAc), 8.88 (s, 5β-Me), 9.00
and 9.12 (C(21)H$_3$ doublet), 9.03 (s, 14β-Me), and 9.12 and
9.22 (side chain methyls) (double irradiation 88 Hz.
downfield caused the C(21)H$_3$ doublet to collapse), M
(mass spectrum) 456.3604 (C$_{30}$H$_{48}$O$_3$ requires 456.3603),
and 6β-acetoxy-3β-methoxy-5,14-dimethyl-18,19-bisnor-
-5β,8α,14β-cholesta-9(10),13(17)-diene (CXX) (21 mg.), a gum,
$\nu_{max.}$ (CHCl$_3$) 1725 (C=O), 1250 (C-O), and 1090 (OMe)cm.$^{-1}$,

τ (CDCl$_3$) 4.86 (m, W½ ca. 18 Hz., 6-H), 6.50 (m, W½ ca.

10 Hz., 3-H), 6.71 (s, OMe), 7.97 (s, OAc), 8.82 (s, 5β-Me),

9.00 and 9.11 (C(21)H$_3$ doublet), 9.07 (s, 14β-Me), and 9.11 and

9.21 (side chain methyls) (double irradiation 87 Hz.

downfield caused the C(21)H$_3$ doublet to collapse). A third

minor product was isolated (35 mg.), a gum, ν max. (CHCl$_3$)

3660, 3450 (OH), 1725 (C=O) and ca. 1240 (C-O) cm.$^{-1}$, τ

(CDCl$_3$) 5.04 (m, W½ ca. 16 Hz., 6-H), 5.53 (m, W½ ca. 11 Hz.,

3-H), 7.97 (s, OAc), 8.90 (s, 5β-Me), 9.02 and 9.12 (C(21)H$_3$

doublet), 9.12 (14β-Me), and 9.12 and 9.22 (side chain methyls)

(double irradiation 87 Hz. downfield caused the C(21)H$_3$ –

doublet to collapse).

The Diene (CXVIIa).- The acetoxy-diene (CXVIIb) (50 mg.) was

hydrolysed and oxidised to give the diene (CXVIIa) (41 mg.),

[α]$_D$+ 132°(c. 0.53), identical with the authentic sample

(by t.l.c., and ^{1}H n.m.r. spectroscopy).

Reaction of the Acetoxy-β-epoxide (CXIIIb).- The epoxide
(600 mg.)
(CXIIIb)/was treated with boron trifluoride for 7 min..

The product mixture was separated by preparative t.l.c.

on silver nitrate impregnated silica (10%) (eluting with

chloroform) to give 6β-acetoxy-3β-methoxy-5-methyl-19-

nor-5β-cholesta-9,11-diene (CXVb) (210 mg.), m.p. 74.5-

76° (from methanol), [α]$_D$- 40.5° (c. 3.95), λ max.

249 n.m., ε max. 25,200, ν max. (CHCl$_3$) 1725 (C=O), ca.

1240 (C-O) cm.$^{-1}$, τ (CDCl$_3$) 3.87 (s, 11,12-H), 5.35

(m, W½ ca. 9 Hz., 6-H), 6.60 (m, W½ ca. 9 Hz., 3-H), 6.79

(s, OMe), 8.03 (s, OAc), 8.84 (s, 5β-Me), and 9.23 (s, 13β-Me)

(Found: C, 78.14; H, 10.50. $C_{30}H_{48}O_3$ requires C, 78.89;

H, 10.59%), 6β-acetoxy-3β-methoxy-5-methyl-19-nor-5β-cholesta-

-1(10), 9(11)-diene (CXVIb)(100 mg.), $[\alpha]_D$- 49.5°(c. 1.40),

$\lambda_{max.}$ 243 n.m., $\varepsilon_{max.}$ 9,200, $\nu_{max.}$ 2830, 1090 (OMe),

1730 (C=O) and ca. 1240 (C-O) cm.$^{-1}$, τ (CDCl$_3$) 4.34 (m,

1,11-H), 5.09 (t, J (apparent) ca. 4 Hz., 6-H), 6.40-7.00

(m, 3-H), 6.78 (s, OMe), 7.99 (s, OAc), 8.92 (s, 5β-Me)

and 9.30 (s, 13β-Me) (Found: C, 78.60; H, 10.52.

$C_{30}H_{48}O_3$ requires C, 78.89; H, 10.59%), and 6β-acetoxy-10-

-hydroxy-3β-methoxy-5,14-dimethyl-18,19-bisnor-5β,8α,9β,14β-

-cholest-13(17)-ene (CXVIIIc) (90 mg.), a gum, $[\alpha]_D$+ 44.5°

(c. 0.68), $\nu_{max.}$ (CHCl$_3$) 3620, 3450 (OH), 1725 (C=O), ca.

1240 (C-O) and 1095 (OMe) cm.$^{-1}$, τ (CDCl$_3$) 4.92 (t, J(apparent)

ca. 8 Hz., 6-H), 6.3-6.8 (m, 3-H), 6.75 (s, OMe),7.95 (s,

OAc), 9.00(s,5β-Me), 9.00-9.12 (C(21)H$_3$ doublet), 9.09 (s,

14β-Me), and 9.12 and 9.22 (side chain methyls) (double

irradiation 90 Hz. downfield caused the C(21)H$_3$ doublet to

collapse) (Found: C, 75.69; H, 10.22. $C_{30}H_{50}O_4$ requires

C, 75.90; H, 10.62%).

Dehydration of the Hydroxy-olefin (CXVIIIc).- The olefin

(CXVIIIc) (9 mg.) in pyridine (1 ml.) at 0° was treated with

thionyl chloride (1 drop) for 5 min.. The mixture was poured

onto crushed ice. Ether extraction gave the diene (CXVIIb)

(8 mg.), identical with the authentic sample (by t.l.c. and

^{1}H n.m.r. spectroscopy).

Reaction of the α-Epoxide (CXIIIg).- The epoxide (620 mg.)

was treated with boron trifluoride for 5 min.. Preparative

t.l.c. of the resultant mixture [eluting (x 3) in benzene]
gave 9-hydroxy-3β-methoxy-cholest-5-ene (CXXI) (54 mg.), m.p.
139° (from methanol), $[\alpha]_D + 9°$ (c. 0.45), $\nu_{max.}$ 3590 (OH)
cm.$^{-1}$, τ 4.66 (m, W$\frac{1}{2}$ ca. 10 Hz., 6-H), 6.4-6.8 (m, 3-H),
6.77 (s, OMe), 8.88 (s, 10β-Me), and 9.42 (s, 13β-Me) (Found:
C, 80.47; H, 11.57. $C_{28}H_{48}O_2$ requires C, 80.71; H, 11.61%),
the ketone (CXIXb) (176 mg.), a gum, $[\alpha]_D -4°$ (c. 0.63), $\nu_{max.}$
1710 (C=O) and 1100 (OMe) cm.$^{-1}$, τ 6.76 (s, OMe), ca. 6.75
(m, 3-H), and 9.04 (s, 5β,13β-Me) (Found: C, 80.57; H, 10.75.
$C_{28}H_{48}O_2$ requires C, 80.71; H, 11.61%), the diene (CXXII)
(108 mg.), a gum, $[\alpha]_D - 18°$ (c. 0.85), $\nu_{max.}$ 1100 (OMe) cm.$^{-1}$,
τ 4.75 (m, W$\frac{1}{2}$ ca. 6 Hz., 6-H), 6.5-7.0 (m, 3-H), 6.79 (s,
OMe), 9.13 (s, 10β-Me), and 9.20 (s, 13β-Me) and 3β-methoxy-
5,14-dimethyl-18,19-bisnor-5β,8α,9β,14β-cholesta-1(10),13(17)-
-diene (CXVIIc) (168 mg.), a gum, $[\alpha]_D + 75°$ (c. 0.66),
$\nu_{max.}$ 1100 (OMe) cm.$^{-1}$, τ 4.93 (m, W$\frac{1}{2}$ ca. 11 Hz., 1-H),
6.53-7.00 (m, 3-H), 6.79 (s, OMe), 8.91 (s, 5β-Me), 9.01 and
9.12 (C(21)H$_3$ doublet), 9.04 (s, 14β-Me), and 9.12 and 9.21
(side chain methyls) (double irradiation 88 Hz. downfield
caused the C(21)H$_3$ doublet to collapse) (Found: C, 84.02;
H, 11.34. $C_{28}H_{46}O$ requires C, 84.35; H, 11.63%).
Hydrogenation of the Diene (CXVIIc).- The diene (CXVIIc)
(80 mg.) as a solution in ethyl acetate (10 ml.) was stirred
under an atmosphere of hydrogen with a palladium-charcoal
catalyst for 3 hr.. The mixture was filtered and the
solvent removed. Preparative t.l.c. of the residue gave
the olefin (CXXIII) (44 mg.), a gum, τ 6.65-7.20 (m,3-H),

6.82 (s, OMe), 9.00 and 9.10 (C(21)H$_3$ doublet) 9.00(s,5β-Me),

9.10(s,14β-Me), and 9.10 and 9.21 (side chain methyls).

Ozonolysis of the Diene (CXVIIc).- A stream of ozone enriched

oxygen was passed through a solution of the diene (CXVIIc)

(100 mg.) in chloroform (20 ml.) at -10° for 45 min.. The

solvent was removed and the residue treated with zinc dust (ca.

100 mg.) in acetic acid (ca. 10 ml.) for 2 hr. at room

temperature. The product was isolated by ether extraction.

Preparative t.l.c. of the crude product [in benzene-ethyl

acetate (3:1)] gave the A,D-diseco-tetrone (CXXIV) (23 mg.)

a gum, [α]$_D$ - 10.5° (c. 0.38), ν $_{max.}$ 2830 (OMe), 2720

(CHO), and 1715 (C=O) cm.$^{-1}$, τ 0.23 (t, J ca. 2.5 Hz.,

CHO), 6.43 (m, W½ ca. 17 Hz., 3-H), 6.81 (s, OMe), 8.50 and

8.87 (angular methyl groups), and 8.93 (d, J ca. 7 Hz., C(21)

H$_3$), M (mass spectrum), 462.3339 (C$_{28}$H$_{46}$O$_5$ requires 462.3345).

Dehydration of the Compound (CXXI).- The hydroxy-olefin (CXXI)

(10 mg.) in pyridine (1 ml.) at 0° was treated with thionyl

chloride (1 drop) for 5 min.. The mixture was poured onto

crushed ice and the product, isolated by means of ether, gave

the diene (CXXVII) (8 mg.), a gum, τ 4.70 (m, 6,11-H), ca.

6.4 (broad m, 3-H), 6.76 (s, OMe), 8.75 (s, 10β-Me), and

9.37 (s, 13β-Me).

Hydrogenation of the Compound (CXXI).- The hydroxy-olefin

(CXXI) (30 mg.) in glacial acetic acid (5 ml.) was stirred

under an atmosphere of hydrogen for 3 hr. with a platinum

catalyst. The mixture was filtered and the solvent removed.

Preparative t.l.c. of the mixture [in benzene-ethyl acetate

127.

(5:1)] gave 3β-methoxy-5α-cholestane (16 mg.), m.p. 83-84.5°

(from methanol), τ 6.81 (s, OMe), 7.03 (m, $W_{\frac{1}{2}}$ ca. 22 Hz.,

3-H), 9.21 (s, 10β-Me) and 9.37 (s, 13β-Me) (lit.,[33] m.p.

82-83°) and 9-hydroxy-3β-methoxy-5α-cholestane (CXXVIII)

(3 mg.), m.p. 130-132° (from petrol), ν max. (CHCl$_3$) 3620,

3450 (OH) and 1100 (OMe) cm.$^{-1}$, τ 6.68 (s, OMe), 6.13-6.70

(m, 3-H), 9.02 (s, 10β-Me), and 9.32 (s, 13β-Me) (Found:

C, 80.51; H, 12.05. $C_{28}H_{50}O_2$ requires C, 80.32; H, 12.04%).

Hydrogenation of the Diene (CXXII).- The diene (CXXII) (50 mg.)

in glacial acetic acid (10 ml.) was stirred under an atmosphere

of hydrogen for 35 min. with a platinum catalyst. The mixture

was filtered and the solvent removed to give the olefin (CXXIX)

(41.5 mg.), a gum, $[\alpha]_D$+ 2.5° (c, 0.93), τ 6.55-7.15 (m, 3-H),

6.80 (s, OMe), 9.13 (s, 10β-Me), and 9.37 (s, 13β-Me), M

(mass spectrum) 400.3694 ($C_{28}H_{48}O$ requires 400.3705).

Use of Eu(D P M)$_3$.- A standard solution of Eu(DPM)$_3$

in carbon tetrachloride (50 mg./ml.) was used. Samples

were made up using a steroid:Eu(DPM)$_3$ ratio of 6:5 w/w..

The results are summarised in Table 2, Section 2,

Discussion 1.

Reaction of the Olefin (CXXIX) with Ruthenium Tetroxide.-

The olefin (CXXIX) (40 mg.) in carbon tetrachloride was shaken

with sodium metaperiodate (100 mg.), ruthenium trichloride

(80 mg.) and water (2 ml.) at room temperature for 1 hr..

The mixture was poured into a sodium sulphite solution. Ether

extraction gave a crude product,which was purified by t.l.c.

[in benzene-ethyl acetate (10:1)] to give the 8,9-seco-dione (CXXXI) (15 mg.), a gum, $\nu_{max.}$ 1705 (C=O) cm.$^{-1}$, τ 6.59 (m, $W\frac{1}{2}$ ca. 10 Hz., 3-H), 6.81 (s, OMe), and 8.89 and 9.01 (angular methyl groups), M (mass spectrum) 432.3604 ($C_{28}H_{48}O_3$ requires 432.3603).

Reaction of the Olefin (CXXIX) with Osmium Tetroxide.- The olefin (CXXIX) (50 mg.) in ether (3 ml.) and pyridine (2 ml.) was treated with osmium tetroxide (ca. 100 mg.) at room temperature for 3 weeks. The mixture was diluted with benzene and saturated with hydrogen sulphide. The mixture was passed through a short alumina column. Removal of the solvent and preparative t.l.c. of the residue [eluting (x 2) in chloroform] gave the diol (CXXX) (33 mg.), an amorphous solid, $\nu_{max.}$ 3600, 3540 (OH), and 1100 (OMe) cm.$^{-1}$, τ 6.80 (s, OMe), 6.91 (m, $W\frac{1}{2}$ ca. 26 Hz., 3-H), 8.90 (s, 10β-Me), and 9.21 (s, 13β-Me), M (mass spectrum) 434.3760 ($C_{28}H_{50}O_3$ requires 434.3760). The diol (CXXX) (33 mg.) in ether (2 ml.) was treated with a solution of periodic acid (20 mg.) in ether (2 ml.) at room temperature for 1 hr.. The mixture was poured into sodium sulphite solution. Ether extraction gave the 8,9-seco-dione (CXXXI) (30 mg.) identical in all respects with the first sample.

Isomerisation of the Olefin (CXXIX).-Dry hydrogen chloride was passed into a solution of the olefin (CXXIX) (2 mg.) in chloroform (5 ml.) for 2 hr. at -30°. The solvent was removed and the residue taken up in glacial acetic acid and stirred under an atmosphere of hydrogen for 12 hr. with a

platinum catalyst. The mixture was filtered and the solvent removed. The mass spectrum (m/e 402, m/e 400) indicated a mixture of fully saturated and olefinic material. The fully saturated material was not 3β-methoxy-5α-cholestane (by t.l.c. comparison with a genuine sample).

Reaction of the β-Epoxide (CXIIIh).- The epoxide (CXIIIh) (318 mg.) was reacted with boron trifluoride for 7 min.. Preparative t.l.c. (in benzene) gave the diene (CXVIIc) (96 mg.), the diene (CXXII) (25 mg.), 3β-methoxy-5-methyl-19-nor-5β-cholesta-9,11-diene (CXVc) (40 mg.), a gum, $[\alpha]_D$- 54° (c. 0.40), $\lambda_{max.}$ 248 n.m., $\mathcal{E}_{max.}$ 27,000, τ 3.89 (s, 11,12-H), 6.59 (m, W½ ca. 9 Hz., 3-H), 6.77 (s, OMe), 8.78 (s, 5β-Me), and 9.24 (s, 13β-Me) (Found: C, 84.19; H, 11.61 $C_{28}H_{46}O$ requires C, 84.35; H, 11.63%), and 9-hydroxy-5-methyl-19-nor-5β,9β,10α-cholestan-3-one (CXXXII) (65 mg.), a gum, $\nu_{max.}$ 3640, 3480 (OH), and 1720 (C=O) cm.$^{-1}$, τ 9.09 and 9.19 (side chain methyls), 9.09(s,5β-Me), and 9.30 (s, 13β-Me), M (mass spectrum) 402.3478 ($C_{27}H_{46}O_2$ requires 402.3498).

Deuteration of the Ketone (CXXXII).- The ketone (CXXXII) (5 mg.) in sodium methoxide-deuteromethanol (ca. 10% solution, 1.5 ml.) was heated in a sealed tube at 80° for 24 hr.. The mixture was cooled and poured into water. Ether extraction gave a single compound, which was subjected to mass spectrometry (see table).

5-Methyl-19-nor-5β-cholest-9(10)-en-3-one (CXXXIIIa).-The hydroxy-ketone (CXXXII) (41 mg.) in pyridine (0.5 ml.) was

treated with thionyl chloride (3 drops) at 0° for 5 min..
The mixture was poured into water and ether extraction gave
the ketone (CXXXIIIa) (36 mg.), a gum, $[\alpha]_D + 14.5^{\circ}$ (c.
0.72), $\nu_{max.}$ 1715 (C=O) cm.$^{-1}$, τ 9.00 (s, 5β-Me), and 9.21
(s, 13β-Me), M (mass spectrum) 384.3372 ($C_{27}H_{44}O$ requires
384.3392).

3β-Methoxy-5-methyl-19-nor-5β-cholest-9(10)-ene (CXIVc).-

The ketone (CXXXIIIa) (35 mg.) in tetrahydrofuran (5 ml.)
was treated with tri-t-butoxy-lithium aluminium hydride (100
mg.) at 0° for 1 hr. with stirring. The mixture was warmed
up to room temperature and the stirring continued for a further
2 hr.. The mixture was poured into water and ether extracted.
Removal of the solvent gave a crude material (pure by t.l.c.),
$\nu_{max.}$ (CHCl$_3$) 3580, 3360 (OH) cm.$^{-1}$. This material was heated
under reflux with finely divided potassium (50 mg.) in benzene
(5 ml.) for 4 hr. under nitrogen. Methyl iodide (2 ml.) was
added and the mixture refluxed for a further 3 hr.. The mixture
was cooled and the excess potassium removed by the addition of
ethanol. The usual work up gave, after t.l.c., the methyl-
ether (CXIVc) (15 mg.), m.p. 59-60° (from ethanol),
$[\alpha]_D + 59.5^{\circ}$ (c.0.3), τ6.60 (m, W½ ca. 10 Hz., 3-H), 6.74
(s, OMe), 8.85 (s, 5β-Me), and 9.22 (s, 13β-Me) (lit.,[28]
m.p. 60°, $[\alpha]_D + 61.7^{\circ}$).

8,9-Epoxy-3β-hydroxy-5α,8α-lanostane (CXXXIXa)[104] -

Epoxidation of the olefin (CXL)[105] (8 g.) gave the epoxide
(CXXXIXa) (7.2 g.), m.p. 157-159° (from ethyl acetate),
$[\alpha]_D + 5^{\circ}$ (c. 1.83) (lit.,[104] m.p. 158-162°, $[\alpha]_D + 7^{\circ}$).

3β-Acetoxy-8,9-epoxy-5α,8α-lanostane (CXXXIXb) [104] – Acetylation

of compound (CXXXIXa) (0.5 g.) gave the epoxide (CXXXIXb)

(0.5 g.), m.p. 140-142° (from ethyl acetate), $[\alpha]_D$+ 14° (c.

0.6), $\nu_{max.}$ 1735 (C=O) and 1240 (C-O) cm.$^{-1}$, τ 5.65 (m,

$W\frac{1}{2}$ 18 Hz., 3-H), 8.05 (s, OAc), 8.89 (s, CH$_3$), 9.10 and

9.19 (d, side chain methyls), 9.19 (s, 3 x CH$_3$), and 9.25

(s, CH$_3$) (lit.[104] m.p. 140-141°, $[\alpha]_D$+ 15°).

Reaction of the 8α,9α-Epoxide (CXXXIXb) with Lewis acids:-

(a) With boron trifluoride for 1 min., the epoxide (CXXXIXb)

(0.5 g.) gave 3β-acetoxy-5α-lanost-7,9(11)-diene (CXL1) (0.4 g.),

m.p. 166.5-167° (from ethyl acetate), $[\alpha]_D$+ 89° (c. 0.8),

$\lambda_{max.}$ 244 n.m., $\epsilon_{max.}$ 13,550, τ 4.63 (m, $W\frac{1}{2}$ 16 Hz., 7-H,

11-H), 5.60 (m, $W\frac{1}{2}$ 18 Hz., 3-H), 8.04 (s, OAc), 9.01 (s, CH$_3$),

9.10 and 9.19 (d, side chain methyls), 9.10 (s, CH$_3$), 9.13

(s, 2 x CH$_3$) and 9.46 (s, CH$_3$) (lit.[106] m.p. 167-168°,

$[\alpha]_D$+ 88°):-

(b) With stannic chloride under the same conditions as above

for 5 min., the epoxide (CXXXIXb) (0.1 g.) gave the

diene (CXLI) (90 mg.).

3β-Acetoxy-9-hydroxy-5α-lanostane (CXLII) [104] – Finely cut

lithium (0.5 g.) was added slowly in portions to a stirred

solution of the epoxide (CXXXIXb) (1.2 g.) in anhydrous

ethylamine (50 ml.). After 2 hr. a blue colour developed.

The reaction was continued for a further hour and was then

quenched by addition of acetone. The mixture was poured into

water and extracted with ether. The ether solution was washed

132.

with dilute hydrochloric acid(2N), saturated sodium

bicarbonate solution and water. The solution was dried

and the solvent removed. The mixture of two products was

acetylated. Preparative t.l.c. [eluting with benzene:ethyl

acetate (10:1)] gave the 9α-hydroxy-compound (CXLII) (0.45 g.),

m.p. 168-169° (from ethyl acetate), $[\alpha]_D+$ 18° (c. 1.5),

$\nu_{max.}$ 3640, 3560 (OH), 1740 (C=O), and 1243 (C-O) cm.$^{-1}$,

Υ 5.68 (m, W½ 18 Hz., 3-H), 8.03 (s, OAc), 8.99, 9.10, 9.15,

and 9.23 (side chain and other methyls) (Found: C, 78.6;

H, 11.5. $C_{32}H_{56}O_3$ requires C, 78.6; H, 11.55%) (lit.[104]

m.p. 163-164°, $[\alpha]_D+$ 7°). (Recrystallisation of an authentic

sample kindly provided by Professor Fried[104] gave

material identical with the above sample). A second fraction

gave the diene (CXLI) (200 mg.). Repetition of this

reaction in the presence of t-butanol (3 or 12 moles/mole of

steroid) gave the same products in the same yields but with

shorter reaction times (30 min. or 10 min. respectively).

3β-Acetoxy-5α-lanost-9(11)-ene (CXLIII)[104] - (a) Thionyl

chloride (0.8 ml.) was added to a solution of the 9α-hydroxy-

-compound (CXLII) (3.8 g.) in pyridine (20 ml.) at 0°.

After 5 min. the solution was poured onto crushed ice and

filtered. The crude product was recrystallised from ethyl

acetate to give the olefin (CXLIII) (3.5 g.), m.p. 174-176°,

$[\alpha]_D+$ 89° (c. 1.3), Υ 4.80 (m, W½ 10 Hz., 11-H), 5.65

(m, W½ 18 Hz., 3-H), 8.05 (s, OAc), 8.94 (s, CH₃), 9.10 and

9.19 (side chain methyls), 9.14 (s, 2 x CH₃), 9.28 and

9.38 (remaining methyl groups) (Found: C, 81.7; H, 11.55 .

$C_{32}H_{54}O_2$ requires C, 81.65; H, 11.55%) (lit.$_{2}$[104] m.p. 162-165°, $[\alpha]_D$+ 85°).

(b) Sulphuric acid (2 drops) was added to a solution of the 9α-hydroxy-compound (0.2 g.) in acetic anhydride (2 ml.) and acetic acid (1 ml.) at room temperature. After 15 min. the solution was poured into brine and the resultant mixture extracted with ether. The ether extracts were washed with sodium bicarbonate solution and water. The solution was dried and the solvent removed. The crude product, separated by preparative t.l.c. [eluting with benzene: ethyl acetate (10:1)] gave the 9α-hydroxy-compound (CXLII) (25 mg.) and the olefin (CXLIII) (150 mg.).

(c) A solution of toluene-p-sulphonic acid (22 mg.) and the 9α-hydroxy-compound (0.1 g.) in acetic anhydride (6.6 ml.) was heated on a boiling water bath for 30 min. and poured into water. The mixture was extracted with ether in the usual way to give the olefin (CXLIII).

<u>3β-Acetoxy-9,11α-epoxy-5α-lanostane</u> (CXLIVa). - The olefin (CXLIII) (1 g.) was epoxidised to give the <u>9,11-epoxide</u> (CXLIVa) (1.1 g.), m.p. 188-189° (from ethyl acetate), $[\alpha]_D$+ 27°(c. 0.85), ν max. 1740 (C=O) and 1245 (C-O) cm.$^{-1}$, τ 5.65 (m, W½ 18 Hz., 3-H), 7.04 (d, J (apparent) <u>ca.</u> 4.8 Hz., 11-H), 8.06 (s, OAc) and 9.17 (m, side chain and other methyls) (Found: C, 78.95; H, 10.85 . $C_{32}H_{54}O_3$ requires C, 78.95; H, 11.2%).

<u>Reaction of the 9,11-Epoxide</u> (CXLIVa) <u>with Lewis acids</u> -

(a) The epoxide (CXLIVa) (0.8 g.) with boron trifluoride for

20 min. gave a mixture. Preparative t.l.c. [eluting with

benzene:ethyl acetate (19:1)] gave 3β-acetoxy-5α,9β-lanostan-

-11-one (CXLVa) (279 mg.), m.p. 199-200° (from methanol/

chloroform), $[\alpha]_D$+ 96° (c. 0.54), $\mathcal{V}_{max.}$ 1740 (acetate

C=O), 1713 (11, C=O) and 1245 (C-O) cm.$^{-1}$, τ 5.50 (m, $W\frac{1}{2}$

19 Hz. 3-H), 8.08 (s, OAc), 9.03, 9.13, 9.23 and 9.25 (side

chain and other methyls) (Found: C, 79.5; H, 11.25

$C_{32}H_{54}O_3$ requires C, 78.95; H, 11.2%), and 3β-acetoxy-8-

-methyl-18-nor-5α,8α,14β-lanosta-9(11),13(17)-diene (CXLVI)

(385 mg.), a gum, $[\alpha]_D$- 18° (c. 0.6), τ (CDCl$_3$, 100 M.Hz.)

4.7 (t, J (apparent) ca. 4 Hz., 11-H), 5.51 (m, $W\frac{1}{2}$ 18 Hz.,

3-H) 7.90 (s, OAc), 9.01 and 9.08 (d, J ca. 7 Hz., C(21)H$_3$),

8.91, 9.03, 9.06, 9.13 and 9.19 (other methyls), and 9.08 and

9.17 (d, side chain methyls) (The doublet at 9.01 and 9.08

collapsed on double irradiation at -149 Hz. to give a broadened

signal at 9.06), molecular weight (mass spectrum) 468.3963

($C_{32}H_{52}O_2$ requires 468.3967), M - side chain 355.2636

($C_{24}H_{35}O_2$ requires 355.2637).

(b) With stannic chloride under the same conditions as above

for 1 hr. the epoxide (CXLIVa) (0.1 g.) gave a mixture of the

ketone (CXLVa) and the $\triangle^{13,17}$- compound (CXLVI) as above.

3β-Acetoxy-5α-lanostan-11-one (CXLVb) - The ketone (CXLVa)

was heated under reflux in ethanol containing sodium ethoxide

for 15 min.. The usual work up gave a crude mixture which

after reacetylation and preparative t.l.c. gave some starting

material (CXLVa) and the ketone (CXLVb), m.p. 150-151°, $[\alpha]_D$

+ 60° (c. 0.5) (lit.$^{(108)}$ m.p. 150-152°, $[\alpha]_D$+ 62°).

3β-Acetoxy-7α-bromo-5α-lanost-8-en-11-one (CXLVIIIa).-

N-Bromoacetamide (0.5 g.) was added over a period of 15 min.

to a stirred solution at 0° of the olefin (CXLIII) (1 g.)

in peroxide free dioxan (10 ml.), perchloric acid (0.74 ml.

aqueous 13% w/v), and water (0.5 ml.).   After a further 2

hr. at room temperature the solution was poured into sodium

thiosulphate solution and the resultant mixture ether extracted.

The ether layer was washed with sodium bicarbonate solution and

water. The solution was dried and the solvent removed. The

product obtained contained a large proportion of starting

material (CXLIII), and was accordingly retreated as above

but for a prolonged period of 14 hr..   The crude product

obtained was chromatographed on deactivated alumina (50 g.)

and gave the olefin (CXLIII) (150 mg.) and the bromo-ketone

(CXLVIIIa) (460 mg.), m.p. 176-177° (from methanol/acetone),

$[\alpha]_D$+ 124° (c. 0.6), $\lambda_{max.}$ (EtOH) 267 n.m., $\varepsilon_{max.}$

7,660, $\nu_{max.}$ 1735 (acetate C=O) 1668 (11$_,$C=O) and 1240

(C-O) cm.$^{-1}$, τ 5.00 (m, W$\frac{1}{2}$ 7 Hz., 7β-H), 5.45 (m, W$\frac{1}{2}$ 19

Hz., 3-H), 8.04 (s, OAc), 8.70, 8.98, 9.1, 9.15, 9.19 and

9.26 (side chain and other methyls) (Found: C, 67.95; H, 8.9;

Br, 14.1 . $C_{32}H_{51}O_3Br$ requires C, 68.2; H, 9.1; Br, 14.2%).

3β-Acetoxy-5α-lanost-8-en-11-one (CXLVIIIb) - A solution of

the bromo-ketone (CXLVIIIa) (88 mg.) in ethyl acetate (5 ml.)

was stirred with a 5% palladium on charcoal catalyst in an

atmosphere of hydrogen at room temperature for 2 hr..   The

solution was filtered and removal of the solvent gave the

ketone (CXLVIIIb) (70 mg.), m.p. 133-134° (from methanol),

$[\alpha]_D$+ 138° (c. 0.6), $\lambda_{max.}$ (EtOH) 257 n.m., $\varepsilon_{max.}$ 9,370, $\nu_{max.}$ 1740 (acetate C=0), 1663 (11, C=0) and 1245 (C-0) cm.$^{-1}$, τ 5.53 (m, W$\frac{1}{2}$ 18 Hz., 3-H), 8.02 (s, OAc), 8.89, 9.08, 9.12 and 9.17 (side chain and other methyls) (Found: C, 78.85; H, 10.4 . $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%) (lit.[108] m.p. 119-120°, $[\alpha]_D$+ 131.3°, $\lambda_{max.}$ 255 n.m., log ε 3.9).

3β,11α-Diacetoxy-5α-lanostane (CXLIXb) and 3β,11α-Dihydroxy--5α-lanostane (CXLIXa). - Finely cut lithium was added to a solution of the ketone (CXLVIIIb) (19.5 mg.) in dry ether (2 ml.) and liquid ammonia (10 ml.) at -40° at a sufficient rate to maintain a blue colouration for 20 min.. Methanol was added and the ammonia allowed to evaporate. Ether and then water was added to the mixture. The organic layer was dried and removal of the solvent gave a crude mixture which was acetylated. Preparative t.l.c. gave the diacetate (CXLIXb) m.p. 128-129° (from methanol) (lit.[113] m.p. 127-128°). Hydrolysis of the diacetate and the usual work up gave the diol (CXLIXa) m.p. 195-198° (from dichloromethane/petrol) (lit.[113] m.p. 195-196°).

Attempted Hydrolysis of the 9,11-Epoxide (CXLIVa). - Treatment of the epoxide (CXLIVa) with (a) aqueous periodic acid/dioxan in a sealed tube at 100° for 2 hr. (b) aqueous dioxan in a sealed tube at 145° for two weeks[115] and (c) aqueous perchloric acid/methyl ethyl ketone[114] failed to give the diol (CXLVIIb). Experiments (a) and (c) gave only the diene (CXLI), while the epoxide (CXLIVa) was unchanged in (b).

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Rel-ative Abundance %	m/e	Formula (Calculated Mass)	Rel-ative Abundance %	m/e	transition
XVIIIf	285		458		14	443		5	428.5	458-443
						383		41	331	443-383
						351		21	322	383-351
						345		10	260	458-345
						253		57	235.5	345-285
									225	285-253
XXII	43		416		19	401		1	354	416-384
						398		2		
						387		1		
						384		4		
						369		1		
						366		1		
						277		9		
XXIV	41		398.3187	$C_{27}H_{42}O_2$ (398.3185)	6	285.1849	$C_{19}H_{25}O_2$ (285.1854)	47		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
XXIXd	268		408			393			318.5	348-333
						348			309	348-328
						333			296.5	408-348
						328			249.5	288-268
						288				
						253			219	328-268
XXXVd	43		388.2562	$C_{24}H_{36}O_4$ (388.2613)		328.2371	$C_{22}H_{32}O_2$ (328.2402)		277.5	388-328
									267	328-296
						313				
						296.2135	$C_{21}H_{28}O$ (296.2140)			
						285				
						281				
						253				

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
XXXVII			436			421			401	436-418
						418			337.5	376-356
						376			324	436-376
						356			277	316-296
						316			266	376-316
						296			246	356-296
XXXVIII	18		388.2608	$C_{24}H_{36}O_4$ (388.2613)	17	328.2394	$C_{22}H_{32}O_2$ (328.2402)	60	277	388-328
						315		8	267	328-296
						296.2135	$C_{21}H_{28}O$ (296.2140)	32		
						281		22		
						255.1752	$C_{18}H_{23}O$ (255.1749)	43		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
XLVd	398		458		6	440		2	362.5	398-380
						429		5	346	458-398
						380		41	342	398-369
						369		66	334	369-351
						351		56	317.5	429-369
XLVe	398		458		3	429		9	346	458-398
						383		6	342	398-369
						380		7	334	369-351
						369		70	317.5	429-369
						351		11		
XLVh	43		458		3	440		2	368	398-369
						398		79	363	398-380
						383		8	346	458-398
						380		9	334	369-351
						369		21	324	380-351
						351		17		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
XLIXa	371		418		0.6	400		20	344	400-371
						353		15	336	371-353
						346		15	292	346-317
						317		7		
LIIa	43					401.3422	$C_{27}H_{34}O_2$ (401.3419)	23		
						370.3230	$C_{26}H_{42}O$ (370.3236)	3		
						341.2837	$C_{24}H_{37}O$ (341.2844)	75		
LIIb	385.3110	$C_{26}H_{41}O_2$ (385.3106)	458.3767	$C_{30}H_{50}O_3$ (458.3760)	10	428.3664	$C_{29}H_{48}O_2$ (428.3654)			
						428.3285	$C_{28}H_{44}O_3$ (428.3290)			
						414.3497	$C_{28}H_{46}O_2$ (414.3498)	25		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LIIIc	414		414.3501	$C_{28}H_{46}O_2$ (414.3498)	100	399		2		
						396.3399	$C_{28}H_{44}O$ (396.3392)	2		
						385.3109	$C_{26}H_{41}O_2$ (385.3106)	3		
						277		20		
LIIId			430			412			368.5	430-398
						401			178	430-277
						398				
						277				
LVIc	28		416.3653	$C_{28}H_{48}O_2$ (416.3654)	4	398.3552	$C_{28}H_{46}O$ (398.3549)	19		
						387		3		
						380.3440	$C_{28}H_{44}$ (380.3443)	8		
						369		8		
						351.3048	$C_{26}H_{39}$ (351.3052)	8		
						285		6		

143.

Mass Spectral Data

| Compound | Base Peak | | Molecular Ion | | | Other Ions | | | | Metastable Peaks |
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LVIIa	351		500.3855	$C_{32}H_{52}O_4$ (500.3865)	1	440 425 411 380 365		4 23 10 42 16	300	411-351
LVIIb	383		412.3355	$C_{28}H_{44}O_2$ (412.3341)		384.3027 383 397 370.3233 365 355.2653	$C_{26}H_{40}O_2$ (384.3028) $C_{26}H_{42}O$ (370.3236) $C_{24}H_{35}O_2$ (355.2637)		356 348	412-383 383-365

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LVIIc	383.3296	$C_{27}H_{43}O$ (383.3314)	472.3819	$C_{31}H_{52}O_3$ (472.3916)	9	443		5	416.5	472-443
						412.3344	$C_{28}H_{44}O_2$ (412.3341)	28	360 351 322	472-412 443-383 383-351
						351.3044	$C_{26}H_{39}$ (351.3052)	85		
LVIIIa	327.2318	$C_{22}H_{31}O_2$ (327.2324)	500.3859	$C_{32}H_{52}O_4$ (500.3865)	13	485 440 425		7 3 34	470 372 313	500-485 485-425 425-365
						387.2526	$C_{24}H_{35}O_4$ (387.2535)	23	276 218	387-327 327-267
						365 267.2117	$C_{20}H_{27}$ (267.2113)	17 72		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LVIIIb	299.2013	$C_{20}H_{27}O_2$ (299.2011)	412.3338	$C_{28}H_{44}O_2$ (412.3341)	7	397		9	357	412-384
						384		37		
						383		38	328	384-355
						355		7	264	299-281
						285.1852	$C_{19}H_{25}O_2$ (285.1855)	13	217	412-299
						281		10		
LVIIIc	345.2430	$C_{22}H_{33}O_3$ (345.2430)	458.3775	$C_{30}H_{50}O_3$ (458.3760)	23	443		27	429	458-443
						398		11	363	398-380
						380		9	310	345-327
						369		7	260	458-345
						327		13	250	285-267
						285.2219	$C_{20}H_{29}O$ (285.2218)	23	235.5	345-285
						267.2112	$C_{20}H_{27}$ (267.2113)	27	218	327-267

146.

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LVIIId	267.2109	$C_{20}H_{27}$ (267.2113)	458.3764	$C_{30}H_{50}O_3$ (458.3760)	19	443 425 383 365 345.2432 327 285.2213	 $C_{22}H_{33}O_3$ (345.2430) $C_{20}H_{29}O$ (285.2218)	22 39 13 35 58 71 42		
LIXa	351		500.3855	$C_{32}H_{52}O_4$ (500.3865)		440.3649 380 365	$C_{30}H_{48}O_2$ (440.3654)		387.5 328 324	500-440 440-380 380-351

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LIXc	412.3703	$C_{29}H_{48}O$ (412.3705)	472.3912	$C_{31}H_{52}O_3$ (472.3916)	14	383.3323	$C_{27}H_{43}O$ (383.3314)	31	360.	472-412
						380.3451	$C_{28}H_{44}$ (380.3443)	38	356	412-383
									351	412-380
									324	380-351
									322	383-351
						351		93		
LXI	43		414.3495	$C_{28}H_{46}O_2$ (414.3498)	13	386		55	359.5	414-386
						342		19	302.5	386-342

148.

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LXVb	43		416.3657	$C_{28}H_{48}O_2$ (416.3654)	17	401		13	387	416-401
						398		7	366	401-383
						383		27	348	383-365
						380		3	268	303-285
						365		6	250	285-267
						303.2315	$C_{20}H_{31}O_2$ (303.2324)	31	220.5	416-303
						285.2218	$C_{20}H_{29}O$ (285.2218)	95	204	398-285
						267.2112	$C_{20}H_{27}$ (267.2113)	26		
LXVc	299.2010	$C_{20}H_{27}O_2$ (299.2011)	412.3335	$C_{28}H_{44}O_2$ (412.3341)	4	397		7	264	299-281
						327		2	217	412-299
						281		5		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LXVe	285		416		8	401		4	366	401-383
						398		21	250	285-267
						383		33	220.5	416-303
						380		8		
						367		10		
						350		8		
						313		5		
						303		11		
						267		88		
LXVI	43		534.3904	$C_{32}H_{54}O_6$ (534.3920)		516			439	474-456
						498				
						474.3697	$C_{30}H_{50}O_4$ (474.3709)		379	414-396
						456.3599	$C_{30}H_{48}O_3$ (456.3603)		361.5	474-414
						445			342	456-396
						414.3488	$C_{28}H_{46}O_2$ (414.3498)			
						396.3398	$C_{28}H_{44}O$ (396.3392)			

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Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LXVIIa	43		532			472			308	419-359
						448			249	359-299
						419				
						359				
						328				
						299				
LXVIc	43		448.3558	$C_{28}H_{48}O_4$ (448.3552)	13	430		17	413	448-430
						415		12	395	430-412
						412		14	300	335-317
						364.2628	$C_{22}H_{36}O_4$ (364.2613)	22	296	448-364
									282	317-299
						335		23		
						317		46		
						299.2023	$C_{20}H_{27}O_2$ (299.2011)	92		

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Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LXVIIIc	355		412.3345	$C_{28}H_{44}O_2$ (412.3341)	16	384.3023	$C_{26}H_{40}O_2$ (384.3028)	9		
						383		8		
LXIX	43		514.3623	$C_{32}H_{50}O_5$ (514.3658)	4	454		45	401.5	514-454
						394		8	342	454-394
						365		6		
LXX	108		414.3494	$C_{28}H_{46}O_2$ (414.3498)		396.3383	$C_{28}H_{44}O$ (296.3392)			
						386.3520	$C_{27}H_{46}O$ (386.3549)			
						386.3140	$C_{26}H_{42}O_2$ (386.3185)			
						371				
						367				
						333				
						320				
						247				

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
LXXIV	43					440.3676	$C_{30}H_{48}O_2$ (440.3654)			
						429				
						369				
						351				
LXXXVIII	297.2230	$C_{21}H_{29}O$ (297.2218)	428.3648	$C_{29}H_{48}O_2$ (428.3654)	17	413		17	398	428-413
						395		42	378	413-395
						363		27	334	395-363
						315.2320	$C_{21}H_{31}O_2$ (315.2324)	29	280	315-297
						265.1956	$C_{20}H_{25}$ (265.1956)	71	236.5	297-265
									232	428-315

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Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
XCa	378.3278	$C_{28}H_{42}$ (378.3286)	470.3770	$C_{31}H_{50}O_3$ (470.3760)	8	455 410.3540 395 384 382 363 357 324 297 265	$C_{29}H_{46}O$ (410.3548)	4 85 15 50 48 18 10 10 25 34	440 358 349 334 272 247.5 236	470-455 470-410 410-378 395-363 470-357 357-297 297-265
XCb	28		426.3502	$C_{29}H_{46}O_2$ (426.3498)	73	398 394 333 305		53 55 58 30	372 364	426-398 426-394

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calcul- ated Mass)	m/e	Formula (Calcul- ated Mass)	Rel- ative Abund- ance %	m/e	Formula (Calcul- ated Mass)	Rel- ative Abund- ance %	m/e	transition
CXVIIa	412		412		100	397 380 365 299 267		3 3 2.5 26 34	238	299-267
CXVIIb			456.3604	$C_{30}H_{48}O_3$ (456.3603)		441 396 381 343 283 251			427 366 329 258 234 223	456-441 396-381 441-381 456-343 343-283 283-251
CXVIIc	285		398		29	383 351 253		21 2 17	368 321.5 225 204	398-383 383-351 285-253 398-285

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Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
CXIXa	43		430.3442	$C_{28}H_{46}O_3$ (430.3448)	24	402.3119	$C_{26}H_{42}O_3$ (402.3134)			
						402.3474	$C_{27}H_{46}O_2$ (402.3497)			
						346.2868	$C_{23}H_{38}O_2$ (346.2872)	31		
CXIXb	120		416		0.7	414		0.66	349	384-366
						384		37		
						366		9		
CXXII	398		398		100	383		11	369	398-383
						366		15	337	398-366
						285		22	225	285-253
						253		6		
						230		23		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
CXXIV			462.3339	$C_{28}H_{46}O_5$ (462.3345)		430 378.2420 362.2815 362.2080 349 346.2138 317	$C_{22}H_{34}O_5$ (378.2406) $C_{23}H_{38}O_3$ (362.2821) $C_{21}H_{30}O_5$ (362.2093) $C_{21}H_{30}O_4$ (346.2144)			
CXXIX	400		400.3694	$C_{28}H_{48}O$ (400.3705)	100	385 368.3449 287.2377	$C_{27}H_{44}$ (368.3443) $C_{20}H_{31}O$ (287.2375)	23 9 13	370 339	400-285 400-368

157.

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Rel- ative Abund- ance %	m/e	Formula (Calculated Mass)	Rel- ative Abund- ance %	m/e	transition
CXXIX Isomerisation	247		402 400		39 21	370 368 387 385 287 248		61 9 45 16 22 20		
CXXX			434.3760	$C_{28}H_{50}O_3$ (434.3760)		416.3652 401 398.3548 384 383 366	$C_{28}H_{48}O_2$ (416.3654) $C_{28}H_{46}O$ (398.3549)		398.5 387.5 382 366 355 336.5	434-416 416-401 416-398 401-383 416-384 398-366

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Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
CXXXI	125.0967	$C_8H_{13}O$ (125.0966)	432.3604	$C_{28}H_{48}O_3$ (432.3603)	38	417 414 400 386 263.2370 221.1901	$C_{18}H_{31}O$ (263.2375) $C_{15}H_{25}O$ (221.1905)	15 11 10 13 27 27	470 397	432-417 432-414
CXXXII			402.3478 $C_{27}H_{46}O_2$ (402.3498)			384 369 333 332 331 330			273/74	402-332

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
CXXXII DEUTERATION			406			388 373 333 332 331 330			270/71	406-332
CXXXIIIa 43			384.3372	$C_{27}H_{44}O$ (284.3392)	12	369 366.3284	$C_{27}H_{42}$ (366.3286)	3.3 0.3	354 348 336 333 277 191	384-369 384-366 366-351 369-351 384-326 384-271
						351 326.2972	$C_{24}H_{38}$ (326.2974)	0.33 1.6		
						313 271		0.47 1.7		

Mass Spectral Data

Compound	Base Peak		Molecular Ion			Other Ions			Metastable Peaks	
	m/e	Formula (Calculated Mass)	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	Formula (Calculated Mass)	Relative Abundance %	m/e	transition
CXLVI	453		468.3963	$C_{32}H_{52}O_2$ (468.3967)	47	408		4	438.5	468-453
						393		12	269	468-355
						355.2636	$C_{24}H_{35}O_2$ (355.2637)	65	245	355-295
						295		8		

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