DISCUSSION
Previous work from these laboratories has described the preparation of several steroidal cyclic acetals from the respective ketones and the lithium aluminium hydride - aluminium chloride (LiAlH₄/AlCl₃) reduction of the former into the corresponding hydroxy ethers. The following chart gives an account of the work carried out in this connection.

\[
\begin{align*}
\text{AcO} & \quad 1. \text{LiAlH}_4/\text{AlCl}_3 \\
\text{[CLXXVI]} & \quad 2. \text{Ac}_2\text{O/Py} \\
\text{[CLXXVII]} &
\end{align*}
\]

Ref. 62

\[
\begin{align*}
\text{[CLXXVIII]} & \quad \text{LiAlH}_4/\text{AlCl}_3 \\
\text{[XXIX]} &
\end{align*}
\]

Ref. 61

\[
\begin{align*}
\text{[CLXXXI]} & \quad \text{w} \\
\text{[CLXXX]} &
\end{align*}
\]

Ref. 61
From the above study on the hydrogenolysis of steroidal cyclic acetics the following salient points of interest may be drawn:

(a) The reaction is steric - approach controlled or kinetically controlled (i.e. where the product is formed regardless of stability consideration).

(b) The reductive cleavage of dioxolane ring follows the accepted mechanism.

(c) $3\alpha,5\alpha$-cyclopropane ring in 6-acetics provides a seat for rearrangement (via a homoallylic cation) and consequently isomeric hydroxyethers were also obtained, besides the expected ethers.

(d) $3\alpha,5\alpha$-cyclopropane ring or a double bond at $C_4-C_5$ in 6-acetics led to the formation of hydrocarbons as products of elimination and/or substitution besides hydroxy ethers, and

(e) In all the cases studied only the corresponding $\beta$-hydroxyethers were obtained except in the case of 6-bromo-3,3-ethylenedioxocholest-5-ene (XXI) where a small amount of the $\alpha$-epimer was also obtained along with the $\beta$-epimer which constituted the major product of the reaction. This difference in the behaviour of the bromoacetatal (XXI) may be explained on the basis of steric hinderance offered by bromine atom at C6 to the incoming reducing species ($AlH_2Cl$) to the reaction site. The preferred course of the attack by $AlH_2Cl$ on the acetal ring
is from the less hindered rear side. The presence of bromine at C6 may offer steric hinderance to the incoming AlH₂Cl from the rear side and therefore a small amount of reactive species may also attack from the front side to give the α-hydroxyether (XXI)⁶⁰.

With this background, the present study was undertaken in order:

(a) to extend the LiAlH₄-AlCl₃ reduction to other unexplored yet easily accessible steroidal cyclic acetals, specially those derived from steroidal diones,

(b) to study the effect of C₄-C₅-double bond on the hydrogenolysis of steroidal bisacetals of 3,6-diones,

(c) to evaluate the synthetic utility of the reactions in steroidal systems and

(d) to check the validity of the accepted mechanism of hydrogenolysis of steroidal cyclic acetals in general.

For the present study 5α-cholestane-3,6-dione (CLXXXIX), cholest-4-ene-3,6-dione (XLVII) and 5-hydroxy-5α-cholestane-3,6-dione (CXC) were selected.
Preparation of Steroidal cyclic acetals.
3,3,6,6-Bisethylenedioxy-5α-cholestan (CXCI).

3,3,6,6-Bisethylenedioxy-5α-cholestan (CXCI) was prepared by the reaction of 5α-cholestan-3,6-dione (CLXXXIX) with ethylene glycol in the presence of catalytic amount of p-toluenesulphonic acid monohydrate. (The dione (CLXXXIX), m.p. 166°C was prepared according to the method described in literature 73). After usual work up of the reaction mixture, the bisacetal (CXCI) was purified by column chromatography and its homogeneity checked by t.l.c. The bisacetal (CXCI), m.p. 120°, analysed correctly for C31H52O4 and its i.r. spectrum showed absorption peaks at 1145, 1039 and 1035 cm⁻¹ (C-O-linkage of the acetal rings). The n.m.r. spectrum of the bisacetal (CXCI) gave signals at δ 3.86 mc (8 protons, C3-O-CH₂-CH₂-O--; C6-O-CH₂-CH₂-O−), δ 0.7, 0.83, 0.93 (methyl protons). Treatment of the bisacetal (CXCI) with aqueous acetic acid regenerated the parent dione (CLXXXIX) quantitatively.

![Chemical structures](CLXXXIX) → (CXCI)
3,3,6,6-Bisethylenedioxycholest-4-ene (CXCI).

- The enedione, cholest-4-ene-3,6-dione (XLVII) used in the present study was prepared according to literature procedure (m.p. 122°, M+ 398, C27H42O2; ) max. 1680s, 1615, 1595 cm⁻¹; max. 252 nm, (€10,300); δ 6.16s (C₄-H), 2.6 mc(C₂-H₂ and C₇-H₂).

The enedione (XLVII) with ethylene glycol in the presence of p-toluenesulphonic acid monohydrate (as catalyst) afforded the bisacetal, 3,3,6,6-bisethylenedioxycholest-4-ene (CXCI) which was purified by column chromatography (t.l.c. homogeneous). The bisacetal (CXCI), m.p. 136°, analysed correctly for C₃₁H₅₀O₄ and its i.r. spectrum showed peaks at 1640 (C=C), 1170, 1134, 1073, and 1034 cm⁻¹ (C-O- linkage of the acetal rings). The n.m.r. spectrum of (CXCI) gave signals at δ 5.85 (1 proton, C₄-H, vinylic proton), 3.85 mc (8 protons, C₃-O-CH₂-CH₂-O-, C₆-O-CH₂-CH₂-O-), 1.2, 0.8, 0.7 (methyl protons). The bisacetal (CXCI) on treatment with aqueous acetic acid or dilute HCl regenerated the parent ketone (XLVII).
5-Hydroxy-3,3,6,6-bisethylenedioxy-5\(\alpha\)-cholestan e (CXCIII).

5-Hydroxy-5\(\alpha\)-cholestan e-3,6-dione (CXC), m.p. 255\(^\circ\), was prepared according to the method described by Fieser.\(^{138}\) The formation of the bisacetal (CXCIII) from the hydroxydione (CXC) with ethyleneglycol and p-toluenesulphonic acid monohydrate (as catalyst) was rather slow and more complicated in comparison with the previous examples. After usual work up of the reaction mixture, it was found to be a mixture of at least 3 components (t.l.c.) and column chromatography provided three distinct products, m.p.ts. 124\(^\circ\), 122\(^\circ\) and 136\(^\circ\).
Characterization of the compound, m.p. 124° as 5-hydroxy-3,3,6,6-bisethylenedioxy-5α-cholestane (CXCI).

The compound, m.p. 124° analysed correctly for C_{31}H_{52}O_{5} and its i.r. spectrum showed absorption peaks at 3550 (sharp, -OH), 1180, 1125, 1086 and 1052 cm⁻¹ (C=O-). The n.m.r. spectrum gave signals at δ 3.9 mc (8 protons, C-3-O-CH₂-CH₂-O-; C-6-O-CH₂-CH₂-O-), 1.06, 0.9, 0.8 and 0.7 (methyl protons).

Characterization of the compound, m.p. 136° as 3,3,6,6-bisethylenedioxycholest-4-ene (CXCI).

The compound, m.p. 136° analysed correctly for C_{31}H_{50}O_{4}. From its composition and m.p. it was obvious that the product at hand was the bisacetal (CXCI) which was previously prepared from the enedione (XLVII). The i.r. and n.m.r. spectra of this product were superimposable with those of the bisacetal (CXCI) obtained in the previous experiment. Further a mixed m.p. determination with (CXCI) showed no depression. It is reasonable to believe that the hydroxydione (CXC) suffered ready dehydration under reaction conditions to give the enedione (XLVII); the latter was subsequently converted into the bisacetal (CXCI).

Characterization of the compound, m.p. 122° as cholest-4-ene-3,6-dione (XLVII).

The compound, m.p. 122° analysed correctly for C_{27}H_{42}O_{2} and from m.p., mixed m.p., i.r. and n.m.r. spectra, this product
was found to be identical with cholest-4-ene-3,6-dione (XLVII)\textsuperscript{73}.

Hydrogenolysis of steroidal bisacetals.

Hydrogenolysis of the bisacetals in the present study was carried out according to published directions\textsuperscript{61,62} using an equimolar mixture of lithium aluminium hydride and anhydrous aluminium chloride in dry diethyl ether. The products of hydrogenolysis were purified by column chromatography and crystallization, and their homogeneity was ascertained by thin layer chromatography. The identification of the products was made with the aid of elemental analysis, i.r. and n.m.r. spectra, and degradative studies.

\begin{align*}
\text{LiAlH}_4\text{-AlCl}_3 & \text{Reduction of 3,3,6,6-bisethylene dioxy-5\textalpha-cholestane (CXCl).} \\
\text{Hydrogenolysis of 3,3,6,6-bisethylene dioxy-5\textalpha-cholestane (CXCl) with LiAlH}_4\text{-AlCl}_3 \text{ (molar ratio 1:1) gave a single product, m.p. 174°, which was identified as 3\textbeta,6\textbeta-(2',2''-bishydroxyethoxy)-5\textalpha-cholestane (CXCIV).}
\end{align*}
The bis-hydroxy ether (CXCV), m.p. 174\(^\circ\)C, analysed correctly for C\(_{31}\)H\(_{56}\)O\(_4\) and its i.r. spectrum showed peaks at 3450 (br, -OH), 1100, 1040 and 1020 cm\(^{-1}\) (C-O-). Its n.m.r. spectrum gave a multiplet centred at $\delta$ 3.66 which integrated for 8 protons attributable to C\(_3\)-O-CH\(_2\)-CH\(_2\)-O- and C\(_6\)-O-CH\(_2\)-CH\(_2\)-O- and another multiplet centred at $\delta$ 3.3 integrating for 2 protons which were assigned to C\(_3\)-H and C\(_6\)-H. Since the C3 and C6 protons are merged together, it was rather difficult to assign the configurations of the ether moieties at C3 and C6 by measuring the half-band widths of C3-H and C6-H peaks. Configurational assignments of ether moieties at C3- as $\beta$ (equatorial) and C6- ($\beta$-axial) at this stage have been made tentatively by analogy\(^60\). Treatment of the hydroxyether (CXCV) with acetic anhydride and pyridine gave 3$\beta$,6$\beta$(2',2''-bisacetoxymethoxy)-5$\alpha$-cholestan (CXCV). The diacetate (CXCV), m.p. 143\(^\circ\)C, analysed correctly for C\(_{35}\)H\(_{60}\)O\(_6\) and its i.r. spectrum gave peaks at 1735, 1240 (CH\(_3\)COO), 1100, 1040, and 1020 cm\(^{-1}\) (C-O-). The n.m.r. spectrum of the diacetate (CXCV) gave signals at $\delta$ 4.16 (dist. t, 4 protons, C3-O-CH\(_2\)-CH\(_2\)-OAc; C6-O-CH\(_2\)-CH\(_2\)-OAc), 3.6 (t, 4 protons, C3-O-CH\(_2\)-CH\(_2\)-OAc; C6-O-CH\(_2\)-CH\(_2\)-OAc), 3.28 (mc, 2 protons C3-H and C6-H), and 2.1 (s; 6 protons C3-O-CH\(_2\)-CH\(_2\)-O-C-CH\(_3\); C6-O-CH\(_2\)-CH\(_2\)-O-C-CH\(_3\)). Again, configurational assignment of ether moieties at C3 and C6 could not be made because of the merger of the C3-H and C6-H signals.
However, the stereochemistry of C3 and C6-ether moieties in the diacetate (CXCV) was determined by following an indirect route. Advantage was taken of the fact that whereas 6α-acetoxyether (equatorial) such as (CXCVI) was cleaved or degraded by BF₃-etherate-acetic anhydride⁶⁴, the 6β-epimer (axial) (CLXXVII) remained indifferent towards this reagent⁶². On the other hand the 3α-acetoxyether (equatorial) (CXCIX) with BF₃-etherate-acetic anhydride gave 3β-acetoxy-5α-cholestanone (CC) as the major product¹³:

\[ \text{AcO} \quad (\text{CXCVI}) \quad \text{BF}_3/\text{Ac}_2\text{O} \quad \text{AcO} \quad (\text{CXCVII}) + \quad \text{AcO} \quad (\text{CXCIX}) \quad \text{BF}_3/\text{Ac}_2\text{O} \quad \text{No change} \quad \text{major product} \quad \text{CC} \]
When subjected to $\text{BF}_3$-etherate-acetic anhydride degradation gave $\text{CXXV}$, as the major product. The diacetate (CXXVII), m.p. 76-77° was found to be identical with an authentic sample of (CXXVIII, m.p., mixed m.p., i.r., n.m.r. and t.l.c. identical). This degradative study is suggestive of the fact that the ether moiety at C3 is equatorial $(\phi)$ whereas at C6 it is axial $(\phi)$. 

\[
\begin{align*}
\text{C}_{17}^1 & \quad \text{H}_17 \\
\text{(CXXV)} & \quad \text{(CXXVII)}
\end{align*}
\]

\text{LiAlH}_4-\text{AlCl}_3. \text{Reduction of } 3,3,6,6-\text{bisethylenedioxycholest-}4\text{-ene (CXCII)}.

The reductive cleavage of the heterocyclic rings in 3,3,6,6-bisethylenedioxycholest-4-ene (CXCII) using the standard procedure gave a mixture of at least 3 components as revealed by t.l.c. Column chromatography of the crude reaction product gave three compounds, m.p. 62°, 126° and 109° and were characterized by usual methods.
The 'Compound' m.p. 62°.

This 'Compound' (CCI) analysed correctly for C_{27}H_{48} (M^+ 372; the fragmentation pattern was similar to cholestanes). It did not give a positive test with tetranitromethane and its i.r. spectrum was devoid of any significant peaks. Its n.m.r. spectrum was featureless in the region 81.8-10. Since its m.p. did not correspond either to 5α-cholestane (m.p. 80°) or 5β-cholestane (m.p. 70°), it was obviously thought to be a mixture of the two. The formation of saturated hydrocarbon is interesting that in the sense whereas the other unsaturated acetal (CLXXXVI) or
the acetal containing 3α,5α-cyclopropane moiety gave products of eliminations as well under reductive conditions, this one \((\text{CXXXVII})\) gave saturated hydrocarbon/s as one of the products.

Characterization of the compound m.p. 126° as 3,5(2',2''-bishydroxyethoxy)cholest-4-ene \((\text{CXX})\).

The compound, m.p. 126° analysed correctly for \(C_{31}H_{54}O_2\) and gave positive test with tetranitromethane. Its i.r. spectrum gave peaks at 3450br(\(\text{OH}\)) 1650 (C=C), 1098, 1067, and 1040 cm\(^{-1}\) (C-O-). Its n.m.r. spectrum gave a doublet like signal at \(\delta 5.9\) integrating for 1 proton ascribable to C4-\(H\) (vinyllic proton) and a multiplet centred at \(\delta 3.73\) integrating for 10 protons \((C3-O-CH_2-CH_2-O; C6-O-CH_2-CH_2-O; C3-H and C6-H)\). The signals
for C3-H and C6-H shifted downfield as compared with the same protons in the saturated homologue (XCIV) where C3-H and C6-H are bunched together at δ 3.3. This is understandable since in the case of the unsaturated ether (XII) both C3-H and C6-H are at allylic positions to C4-C5 double bond. Since the signals for C3-H and C6-H merged with other signals, it was not possible to ascertain the configurations of C3- and C6-ether moieties.

Treatment of the bishydroxyether (XII) with acetic anhydride gave the corresponding diacetate (XIII) as a non-crystallizable oil (purified by column chromatography, homogeneous by t.l.c.). The diacetate (XIII) analysed correctly for C_{35}H_{58}O_6 and its i.r. spectrum showed peaks at 1736, 1235 (CH_3 - C - O-), 1650 (C=C), 1100, 1040, and 1025 cm^{-1} (C-O-). The n.m.r. spectrum of the diacetate (XIII) gave signals at δ 5.88 (doublet like, 1 proton, C4-H), 4.1 mc (triplet like, 4 protons, C3-O-CH_2-CH_2-OAc; C6-O-CH_2-CH_2-OAc), 3.8 mc (2 protons, C3-H and C6-H), 3.55 (triplet like, 4 protons, C3-O-CH_2-CH_2-OAc; C6-O-CH_2-CH_2-OAc), 2.01s (3 protons) and 2.07s (3 protons) (C3-O-CH_2-CH_2-O-C-CH_3 and C6-O-CH_2-CH_2-O-C-CH_3).

Again the signals for C3-H and C6-H are merged together and therefore configurational assignments of C3- and C6-ether moieties could not be made by measuring half-band widths of C3-H and C6-H signals. However, by analogy, the configurations of the ether moieties have been assigned as C3e-(equatorial) and C6e-(axial).
Characterization of the compound, m.p. 109° as 3β-(2'-hydroxyethoxy)-5α-cholestan-6-one (CCIV).

The compound, m.p. 109° analyzed correctly for C_{29}H_{50}O_{3} and its i.r. spectrum showed peaks at 3550(OH), 1710 (C=O), 1098, 1062 and 1040 cm\(^{-1}\) (C-O-). The presence of a saturated carbonyl group in the compound suggested that the reduction was complicated in the sense that only one of the acetal ring systems suffered hydrogenolysis together with the reduction of C4-C5 double bond. The remaining acetal ring on subsequent work up with dilute H_{2}SO_{4} regenerated that ketone moiety. This leads to two possibilities (CCIV) and (CCVI).

That the product was not a mixture was ascertained by t.l.c. in different solvent systems. The n.m.r. spectrum of the compound, m.p. 109°C, gave signals at 6 3.7 mc (4 protons) ascribable to C3-O-CH_{2}-CH_{2}- or C6-O-CH_{2}-CH_{2}-O-; 3.1br (1 proton) C3-H or C6-H and 2.25 mc (2 protons; -CH_{2}-). There was no indication of a vinylic proton. The magnitude of splitting of the peak centred
at $\delta 3.1$ with half band width of 16 Hz suggested that this proton is axial and that it is interacting with at least 4 protons (2 axial and 2 equatorial protons). Further the signal at $\delta 2.2$ integrating for 2 protons suggested the presence of one methylene group $\alpha$- to a carbonyl group. These observations strongly suggested that the compound, m.p. 109$^\circ$ has the structure (CCIV). On steric ground also, it is to be expected that the acetal ring system concerned with C3 will be preferentially hydrogenolysed in comparison to the one at C6.

The keto-hydroxyether (CCIV) was readily converted into its acetate (CCV), m.p. 105$^\circ$, on treatment with acetic anhydride and pyridine. The keto-acetate (CCV), analysed correctly for $^{0}_{1}$C$_{31}$H$_{52}$O$_{4}$ and its i.r. spectrum gave peaks at 1736, 1235 (CH$_{3}$ -C -O-) and 1710 (C=O). The n.m.r. spectrum gave signals at $\delta 4.1\alpha$ (2 protons, C3-O-CH$_{2}$-CH$_{2}$-OAc), 3.70t (2 protons, C3-O-CH$_{2}$-CH$_{2}$-OAc), 3.1br (1 proton, $\frac{1}{2}$Hz, C3-H, $\alpha$-axial), 2.3 mc (2 protons, CH$_{2}$-C-), and 2.0s (3 protons, -O-C-CH$_{3}$).

From the n.m.r. spectra of the ketoether (CCIV) and ketoacetate (CCV), it is obvious that the configuration of the ether moiety at C3 is equatorial ($\beta$-oriented). This conclusion was further supported by the degradative studies. The keto-acetate (CCV) on treatment with BF$_{3}$-etherate-acetic anhydride provided 3$\beta$-acetoxy-5$\alpha$-cholestan-6-one (CXV) as the major product. This
not only helped in the assignment of the configuration of the ether moiety but also supported the structure of the ketoacetate as (CCV).

\[
\text{BF}_3\cdot\text{Ac}_2\text{O} \rightarrow \text{AcO}^{-}\]

The formation of the saturated hydrocarbon/s (CCI) and the keto-ether (CCIV) from the hydrogenolysis of the bisacetal (CXCI) is intriguing. A tentative mechanism for the formation of (CCI) and (CCIV) is given below. Apparently, one or more pathways have to be considered to account for 3 products of hydrogenolysis. According to the accepted mechanism of hydrogenolysis of steroidal cyclic acetals by LiAlH\(_4\)-AlCl\(_3\), the bisacetal (CXCI) is attacked by reducing agent (AlH\(_2\)Cl) at the rear oxygen atoms of the acetal moieties at C3 and C6 leading to the normal product, i.e. the bis-hydroxyether (CCII). This then suffers further changes to give the hydrocarbon product (CCI).

On the other hand, the bisacetal (CXCI) may be attacked preferentially at C3-acetal moiety and this course then can lead to the C3-acetal ring cleavage and reduction of C4-C5 double bond.
\( \alpha \)-Bromination of 3\( \beta \)-acetoxy-5\( \alpha \)-cholestan-6-one (CXV)

In order to prepare 3\( \beta \)-acetoxy-5\( \alpha \)-cholesta-7-en-6-one (CCVIII) according to the following scheme, the preparation of 3\( \beta \)-acetoxy-7\( \alpha \)-bromo-5\( \alpha \)-cholestan-6-one (CCVII) was undertaken according to the method described by Héilbron and coworkers since they studied the mono- and dibromination of the title compound (CXV)\(^{73,76}\).

When 3\( \beta \)-acetoxy-5\( \alpha \)-cholestan-6-one (CXV) was treated with \( \text{Br}_2/\text{HBr} \) in ether-acetic acid under reflux for 2 hours and the reaction mixture, after removal of the ether solvent, set aside for 24 hours, it invariably afforded a product, m.p. 186\(^\circ\), after column chromatography and crystallization. In one or two experiments, under similar conditions, a product, m.p. 140\(^\circ\), was obtained. None of these products was found to be the desired 7\( \alpha \)-bromoketone (CCVII).
Characterization of the compound, m.p. 186° as 3β-acetoxy-5,7,7-tribromo-5α-cholestan-6-one (CCIX).

The compound, m.p. 186° (positive Beilstein test) analysed correctly for C_{29}H_{45}OBr_{3}. From the composition, it is evident that 3 bromine atoms were introduced at α-positions to the C6-carbonyl group. The i.r. spectrum of the compound (CCIX) gave peaks at 1739, 1221 (CH₃-COO-), 1720 (C=O) and 750 cm⁻¹ (C-Br)¹⁴³. Its n.m.r. spectrum (100 MHz) gave signals at δ 5.4m (1 proton C3-H, axial, α-oriented, 7-peaks J = 10 and 5 Hz)¹⁴¹, 2.05s (3 protons, CH₃-COO), 1.05 (C10-Me), 0.78 (C13-Me), 0.98, 0.92 and 0.85 (other methyl protons); no other signal was observed in the region δ 2.5-10.

![Chemical structures](image)

The signal for C3-H appeared at relatively low field i.e. at δ 5.4. Generally the C3-H (α, axial) in compounds of the type (CXV) gives signal at about δ 4.7-5. This downfield shift of C-3H signal in the tribromide (CCXI) led to the suspicion that Br
at C5 is β (equatorial, A/B ring junction cis), thus causing C3α-H to be equatorial, which would appear in the downfield region (structure CCXI). In order to remove this doubt, the n.m.r. spectrum of the known 5α-bromocompound, 3β-acetoxy-5-bromo-5α-cholestan-6-one (CCXII) was determined.

![Chemical Structures]

The n.m.r. spectrum (100 MHz) of the 5α-bromoketone (CCXII) gave signals at 5.35m (1 proton, C3-H, axial, β, 7-peaks, J=10 and 5 Hz), 2.3d like (2 protons, C7-H2-O-2) 2.02s (3 protons, CH3-COO-), 1.0 (C10-Me), 0.7 (C13-Me), 0.92 and 0.83 (other methyl protons). The striking similarity between the signals of C3-H protons in the tribromide (CCIX) and 5α-bromoketone (CCXII) in terms of splitting magnitude and shape leaves no doubt that in the tribromide (CCIX), the C5-Br is axial. The downfield shift of C3-H may be attributed to the presence of C5α-Br. It is pertinent to mention that in steroidal C3-acetate (β-equatorial) the signal for C3-H (α'-axial) appears as septet
with J=10 and 5 Hz, in 100 MHz spectrum, though at a higher field (say in the region $\delta 4.7-5$).

**Characterization of the compound, m.p. 140° as 3\(\beta\)-acetoxy-5,7\(\alpha\)-dibromo-5\(\alpha\)-cholestan-6-one (XLV).**

The compound, m.p. 140°, analysed correctly for C\(_{29}\)H\(_{46}\)O\(_3\)Br\(_2\) (positive Beilstein test) and its i.r. spectrum showed peaks at 1732, 1250 (CH\(_3\)COO\(^-\)), 1710 (C=O), and 750 cm\(^{-1}\) (C-Br). Heilbron and coworkers\(^7\), have reported the m.p. 129° for the dibromide (XLV) and 145° for 3\(\beta\)-acetoxy-7\(\alpha\)-bromo-5\(\alpha\)-cholestan-6-one (CCVII). The closeness in m.p.ts. of our compound (140°) and that of 7\(\alpha\)-bromo compound (CCVII) indicated the possibility that the compound m.p. 140° could be 7\(\alpha\)-bromo compound. However, elemental analysis eliminated this possibility. Further, the m.p. of 3\(\beta\)-acetoxy-5, 7\(\alpha\)-dibromo-5\(\alpha\)-cholestan-6-one (XLIV) is reported to be 152°.
The n.m.r. spectrum (100 MHz) of the compound, m.p. 140°, was very decisive in arriving at a definite conclusion. It gave signals at δ 5.37d (J=9.5 Hz, 1 proton, C7-H, axial, δ-orientated), 5.25br,m (1 proton, C3-H, axial, δ-orientated), 2.04s (3 protons, CH₃-COO⁻), 0.98 (C10-Me), 0.70 (C13-Me), 0.95, 0.9 and 0.83 (other methyl signals). The appearance of a doublet (J=9.5 Hz) at δ 5.37 and a broad multiplet centred at δ 5.25 leaves no doubt as to the correctness of the structure (XLV) assigned to the compound, m.p. 140°. In the absence of a C5δ(-bromine the C3 proton was likely to give signal at about δ 4.7. Although the signals at δ 5.37 and 5.25 were overlapping in part, nevertheless they were clearly discernible. The structure of the dibromide (XLV) was further supported by dehydrobromination (refluxing pyridine) when it gave the known compound 3-acetoxycholesta-2, 4-dien-6-one (XLVI), reported earlier.

**Dehydrobromination of 3α-acetoxy-5,7,7-tribromo-5α-cholestan-6-one (CCIX).**

The tribromide (CCIX), m.p. 186°, was subjected to dehydrobromination with refluxing pyridine and after usual work up of the reaction mixture it gave two compounds as revealed by t.l.c. Column chromatography of the crude reaction product afforded two well defined crystalline products, m.p. 139° and 123°, respectively.
Characterization of the compound, m.p. 139\(^\circ\) as 3-acetoxycholest-2,4-dien-6-one (XLVI).

The compound, m.p. 139\(^\circ\) (negative Beilstein test) analysed correctly for \(\text{C}_{29}\text{H}_{44}\text{O}_{3}\) and its i.r. spectrum showed peaks at 1755 (CH\(_3\)-C-O-C=C, \(\text{enol acetate}\)), 1675 (\(\text{C}=\text{C}-\text{C}=\text{O}\)), 1645 (\(-\text{O}-\text{C}=\text{C}\)), 1570 (\(\text{C}=\text{C}\)), and 1250 cm\(^{-1}\) (acetate). Its u.v. spectrum showed absorption maxima at 317 nm (reported \(\lambda_{\text{max}}\) 317 nm). The n.m.r. spectrum displayed signals at \(\delta 6.57\) (d, \(J=1.5\) Hz, 1 proton \(\text{C}4\)-H; long range coupling with \(\text{C}2\)-H, \(\wedge\) pattern), 5.67t (each splits into doublet, 1 proton, \(J=1.5\) Hz, \(\text{C}2\)-H), 2.4d like (2 protons, \(\text{CO}-\text{CH}_2\)-\(\text{C}3\)-H), 2.05s (3 protons, \(\text{CH}_3\)-\(\text{COO}\)), 1.1 (\(\text{C}10\)-Me), 0.7 (\(\text{C}13\)-Me), 0.92, 0.90, 0.83 (other methyl signals).

The mass spectrum of the dienone acetate (XLVI)(Fig. 1) is very revealing and gave molecular ion peak at m/e 440 (\(\text{C}_{29}\text{H}_{44}\text{O}_{3}\)), with other significant peaks at m/e 425 (M-\(\text{CH}_3\)), m/e 412 (M-\(\text{CO}\)), m/e 398 (base peak; M-\(\text{CH}_2=C=O\)), m/e 383 (m/e 398-\(\text{CH}_3\)) and lower
mass peaks. The fragment ion m/e 398 (base peak) showed that the molecular ion loses a molecule of ketene (CH$_2$=C=O) and this assumption is well supported by a metastable peak at 360. The loss of a ketene molecule supports the presence of an enol acetate function; the loss of ketene is of common occurrence in enol acetates.

![Diagram](image)

(XLVI) m/e 398

As anticipated the molecular ion did not show the loss of acetic acid since this would have involved two vinylic bonds cleavage, which is not considered to be a favourable process. (Loss of acetic acid from acetates occurs by 1,2-elimination).

The fragment ion peak at m/e 383 (m/e 398-CH$_3$) is also very pronounced and arises by the loss of a methyl group from the fragment ion m/e 398. This is supported by a metastable peak at 368.56. The M-CO peak at m/e 412 is very weak as the loss of CO from the molecular ion will involve the cleavage of
a vinylic bond at one stage or the other.

\[ (XLVI^m) \]

\[ \text{AcO} \]

\[ \text{AcO} \]

\[ (vinylic \ bond \ cleavage) \]

\[ \text{AcO} \]

\[ \text{AcO} \]

\[ \text{m/e 412} \]

Or

\[ \text{AcO} \]

\[ \text{AcO} \]

\[ \text{m/e 412} \]
Mild hydrolysis of 3-acetoxycholesta-2,4-dien-6-one (XLVI) gave the known compound, cholest-4-ene-3,6-dione (XLVII).  

\[
\text{\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure}
\end{figure}}
\]

From the foregoing arguments it is evident that the compound m.p. 139° is 3-acetoxycholesta-2,4-dien-6-one (XLVI).

Characterization of the compound, m.p. 123° as cholest-4-ene-3,6-dione (XLVII).

The compound, m.p. 123°, (negative Beilstein test) analysed correctly for C\(_{27}H_{42}O_2\) and its i.r. spectrum showed absorption bands at 1680 (C=C-C=O), 1615 and 1595 cm\(^{-1}\) (C=C-C=O). The presence of enedione moiety was further revealed by its u.v. spectrum (\(\lambda_{\text{max}}\) 252 nm, \(\epsilon_{11,000}\); reported \(\lambda_{\text{max}}\) 253 nm, \(\epsilon_{11,200}\)). Its n.m.r. spectrum exhibited signals at \(\delta\) 6.16s (1 proton, C4-H), 2.0-2.4m (4H, C2-H\(_2\) and C7-H\(_2\)), 1.1 (C10-Me), 0.70 (C13-Me), 0.92, 0.90, and 0.83 (other methyl signals). The mass spectrum of (XLVII)(Fig. 2) gave molecular ion peak at m/e 398 (C\(_{27}H_{42}O_2\)), followed by significant peaks at m/e 383(M-CH\(_3\)),...
Figure 2

Relative Intensity

m/e

0 40 80 120 160 200 240 280 320 360 400

356 (M-CH₂=CO)
370 (M-CH₂=CO)
380 (M-H₂O)
383 (M-CH₃)
398 (M-CH₂=CH)

267
247
243

285 (M-CH₃)

152

137 (C₂H₉O₂)
C₂H₄O₂

M+ 396

C₈H₁₇
m/e 380 (M-H₂O), m/e 370 (M-CO), m/e 356 (M-CH₂⁻C=O), m/e 285 (M-C₈H₁₇), m/e 267, m/e 257, m/e 247, m/e 244, m/e 243, m/e 152, m/e 137 (base peak) and lower mass peaks. The formation of some of the salient fragment ions has been given below.

m/e 383 and m/e 380. These fragment ions represent the loss of a methyl group and a molecule of water, respectively from the molecular ion, and are supported by metastables at 368.5 and 362.8.

m/e 370 (C₂₆H₄₂O). The fragment ion m/e 370 represents the loss of CO from the molecular ion and is supported by a metastable peak at 343.9. The loss of CO may involve either the C₃ or C₆ carbonyl function or both. In either case, this loss involves the cleavage of a vinylic bond at one stage or the other. Several possibilities exist for the elimination of CO from the molecular ion. However, only one mechanism is being given below.
The fragment ion m/e 356 is best represented by the loss of a molecule of ketene from the molecular ion and this is supported by a metastable at 318.4. \( \alpha,\beta \)-Unsaturated ketones, specially those having alkyl substituents at position 4 relative to the carbonyl group give intense \( \text{M-CH}_2\text{=C}=\text{O} \) peak. The C3 keto group at its relative position 4 is more substituted than the C6 keto group in this respect and therefore, is likely to contribute more in the expulsion of ketene molecule from the molecular ion. Thus fragmentation mode A is likely to contribute more than the mode B as shown below.

---

\[ \text{m/e 285} \]
This fragment ion obviously results by the loss of the side chain \((\text{C}_8\text{H}_{17})\) from the molecular ion.

\[ \text{m/e 257} \]
The fragment ion m/e 257 can be formulated as given below, which results by the elimination of the side chain and part of ring D.
This hydrocarbon fragment ion is of common occurrence in the mass spectra of the cholestane derivatives. In the present case, its genesis has been rationalized according to pathway suggested below.

These fragment ions can be rationalized according to scheme given below.
m/e 244

m/e 243

m/e 137 (base peak: \( \text{C}_8\text{H}_9\text{O}_2 \)). This is the base peak of the spectrum and its composition suggested that this must encompass both C3 and C6 carbonyl groups. A probable mechanism has been suggested below.
From these observations it was evident that the compound, m.p. 123°, is cholest-4-ene-3,6-dione (XLVII) which was further confirmed by comparison with an authentic sample prepared according to the literature method. Both the samples were found to be identical in all respects. Cholest-4-ene-3,6-dione (XLVII) in all probability is an artefact of 3-acetoxycholesta-2,4-dien-6-one (XLVI).
Dehydrobromination of 3β-acetoxy-5,7β-dibromo-5α-cholestan-6-one (XLV).

The dehydrobromination of 3β-acetoxy-5,7β-dibromo-5α-cholestan-6-one (XLV) was carried out in a manner described for the tribromide (CCIX). After usual work up of the reaction mixture, followed by column chromatography, 3-acetoxycholesta-2,4-dien-6-one (XLVI) and its artefact, cholest-4-ene-3,6-dione (XLVII) were obtained, comparable with the previously obtained samples in all respects.

It is pertinent to mention that the dibromide (XLV) on dehydrobromination with pyridine was reported to furnish 3β-acetoxy-β-norcholest-5-en-6-carboxylic acid (LI) along with 3-acetoxycholesta-2,4-dien-6-one (XLVI).78

In our experiment, we were unable to isolate the β-nor carboxylic acid (LI). The acid (LI) if formed must have been in small quantity as to escape isolation.
Although the formation of 3-acetoxycholesta-2,4-dien-6-one (XLVI) from 3\(\beta\)-acetoxy-5,7\(\beta\)-dibromo-5\(\alpha\)-cholestan-6-one (XLV) was reported earlier, its mechanism was not given in detail. The more intriguing is the formation of (XLVI) from the tribromide, 3\(\beta\)-acetoxy-5,7,7-tribromo-5\(\alpha\)-cholestan-6-one (CCIX). The conversion (CCIX) \(\rightarrow\) (XLVI) requires that \(\alpha\)-debromination occurs at one stage or another under reaction conditions. A tentative mechanism is now being proposed to account for the formation of 3-acetoxycholesta-2,4-dien-6-one (XLVI) from the tribromide (CCIX).
It is pertinent to mention that a similar observation was made by Schwenk and Whitman when they obtained cholestan-3-one (CCXIII) from 2α-bromocholestan-3-one (XXXVI) on heating the latter with N,N-dimethylaniline.

In our continued efforts to prepare 3β-acetoxy-7α-bromo-5α-cholestan-6-one (CCVII) from 3β-acetoxy-5α-cholestan-6-one (CXV), the latter was heated under reflux with bromine and HBr (as catalyst) in the solvent system ether-acetic acid for 22 hours. After usual work-up of the reaction mixture, followed by chromatography, 3β-acetoxy-5α-bromocholestan-6-one (CCXII), m.p. and mixed m.p. 162–163° and compounds, m.p's. 140° and 172°, were obtained. The identity of the compounds, m.p's. 140° and 172° was made on the basis of spectral properties, elemental analysis and comparison with authentic sample where available.
Characterization of the compound, m.p. 140° as 1-methyl cholesta-1,3,5(10)-trien-6-one (CCXIV).

The compound, m.p. 140° (negative Beilstein test) analysed correctly for $C_{27}H_{40}O$ and its i.r. spectrum showed absorption bands at 3030w, 1585m(aromatic), 1680s cm$^{-1}$ ($\equiv\equiv$C-C=O). There was no peak corresponding to acetate group either in the region 1730 or 1200 to 1250 cm$^{-1}$. The presence of an aromatic ring system conjugated with a carbonyl group was further substantiated by its u.v. spectrum ($\lambda$ max. 255 nm; together with another band at 335 nm (weak).

\[
\begin{align*}
\text{AcO} & \xrightarrow{\text{Br}_2/HBr} \text{AcO} \\
\text{Ether-AcOH} \Delta , 22 \text{ hrs} & \rightarrow \text{AcO} + \text{phenol}
\end{align*}
\]

The presence of an aromatic ring system was further revealed by the n.m.r. spectrum of the compound, m.p. 140°. The n.m.r. spectrum exhibited signals at $\delta$ 7.9, d,d ($J=8$ Hz, ortho coupled, and 3 Hz meta coupled, 1 proton, C4-H), 7.26m (2 protons, C2-H and C3-H), 2.43s (3 protons; C1-CH$_3$), 2.5m (merging with the methyl signal, $-\text{C-CH}_2$), 0.71 (C13-Me), 0.9 and 8.3 (other methyl
protons). The appearance of signals in the downfield region i.e. δ7.9 and 7.26 clearly indicated the presence of an aromatic ring in the compound under discussion. Two possible structures (CCXIV) and (CCXV) can be written for the compound, m.p. 140°.

A distinction between these structures (CCXIV) and (CCXV) was made with the help of n.m.r. spectrum. As is obvious from the structure (CCXIV), it has one β-proton with respect to the carbonyl function at C6 whereas in the other structure (CCXV), the β-position is occupied by a methyl group. The appearance of a signal at δ7.9 clearly indicated that there is a β-proton with respect to the carbonyl group compatible with the structure (CCXIV). In the other structure (CCXV) all the 3 aromatic protons are expected to be appearing as a multiplet at about δ7.3. On this basis the structure (CCXIV) has been assigned to the compound, m.p. 140°. A comparison of the n.m.r. values of the compound (CCXIV) was made with that of 1-methyl-1-
carboxymethyl-4-tetralone (CCXVI), where the $\beta$-proton to the carbonyl group appeared at downfield relative to other aromatic protons.

\[
\begin{align*}
\text{CH}_2\text{COOH} & \quad H(7), H(8), H(9) - \delta 7.41 \\
\text{H}(10) & \quad \delta 8.02
\end{align*}
\]

(CCXVI)

The compound, m.p. 172° (M$^+$ 400, C$_{27}$H$_{44}$O$_2$; C=O 1710 cm$^{-1}$; 2.3m (6 protons, C$_2$-H$_2$, C$_4$-H$_2$, and C$_7$-H$_2$), 0.96 (C$_{10}$-Me), 0.71 (C$_{13}$-Me), 0.92 and 0.83 (other methyl signals) was identified as 5$\alpha$-cholestane-3,6-dione (CLXXXIX) by comparison with an authentic sample, prepared according to the literature procedure. The formation of the dione (CLXXXIX) may be rationalized according to the following sequence of reactions.
An account for the formation of the ring A aromatized product, 1-methyl-cholesta-1,3,5(10)-trien-6-one (CCXIV) from 3β-acetoxy-5α-cholestan-6-one (CXV) demands serious considerations. It has been experimentally realized that 3β-acetoxy-5α-bromocholestan-6-one (CCXII) gives rise to the aromatized product (CCXIV) under similar reaction conditions.

\[ \text{(CCXII)} \rightarrow \text{(CCXIV)} \]

It has been recently observed by Hanson that 2α,3α-epoxy-5α-hydroxyandrostan-17-one (LXXVIII) undergoes rearrangement to form 4-methylestra-1,3,5(10)-trien-17-one (LXXVII) whilst the corresponding 6-ketone (LXXIX) affords 1-methylestra-1,3,5(10)-triene-6,17-dione (LXXX) on treatment with HBr in glacial acetic acid.

\[ \text{(LXXVIII)} \rightarrow \text{(LXXVII)} \]
The presence of a 6-carbonyl function serves, as in the dienone-phenol rearrangement, to destabilize a C5-carbonium ion and prevents the formation of spirocyclic intermediates. This leads to aromatization via the alternative pathway of C10 \( \rightarrow \) C1 methyl migration.

Further the prerequisite for aromatization of ring A is the presence of three potential sites of unsaturation in rings A and B\(^{93,98}\).

In view of these observations any postulated mechanism should avoid the formation of a C5-carbonium ion and subsequent spirocationic intermediate formation in the conversion (CXV) \( \rightarrow \) (CCXIV) and should involve such intermediate/s which have 3 potential sites of unsaturation in rings A and B.

The following mechanism, though tentative, is being proposed for the formation of the aromatized product (CCXIV).
1,3-Hydride shift

$\text{AcO}$

$\text{Br}^-\text{HBr}$

$\text{H}^+$

1,2-Hydride shift

$\text{H}_2\text{O}^+$

1,2-Methyl migration

$\text{H}^+$
Baeyer-Villiger Oxidation of Steroidal Ketones

Previous work from these laboratories described the perbenzoic acid oxidation of 3\(\beta\)-acetoxycholest-5-en-7-one (CLXIII), cholest-5-en-7-one (CLVIII), 3\(\beta\)-halo-5\(\alpha\)-cholestan-6-ones (CLVII), (CLVIII) and (CLIX), 3\(\alpha\),5-cyclo-5\(\alpha\)-cholestan-6-one (CLV) and 6\(\beta\)-bromocholest-4-en-3-one (CLXX).
In view of obtaining some interesting results and to extend the above work, cholesta-3,5-dien-7-one (CCXVII) was subjected to Baeyer-Villiger oxidation.

**Reaction of cholesta-3,5-dien-7-one (CCXVII) with perbenzoic acid.**

Reaction of the dienone (CCXVII) with perbenzoic acid using p-toluenesulphonic acid gave, after usual work up procedure and chromatography, two compounds, m.p. 136° and 205°. These were identified as 3α,4α-epoxycholest-5-en-7-one (CCXVIII) and 3α,4β-dihydroxycholest-5-en-7-one (CCXIX), respectively on the basis of chemical and spectral evidence.

The compound (CCXVIII), m.p. 136°, analysed correctly for \(\text{C}_{27}\text{H}_{42}\text{O}_2\) and its mass spectrum gave molecular ion peak at m/e 398 (C\(_{27}\text{H}_{42}\text{O}_2\)). From elemental composition it is apparent that only one oxygen atom has been introduced during the reaction. This leads to several possibilities and the product may be formulated as the epoxide (CCXVIII), the enol lactone (CCXXI), or the \(\alpha\beta\)-unsaturated lactone (CCXXII).
The u.v. spectrum of the product ($\lambda_{\text{max}}$ 241 nm, log ε 3.46), showed the presence of an $\alpha$, $\beta$-unsaturated ketonic function. The presence of an $\alpha$, $\beta$-unsaturated ketonic group was further supported by its i.r. spectrum. The i.r. spectrum showed peaks at 1680 (C=C=C=O), 1638 (C=C=), 870 and 775 cm$^{-1}$ (epoxide ring$^{143}$). These spectral properties clearly discarded the $\xi$-lactone structures (CCXXI) and (CCXXII). Further the n.m.r. spectrum of the compound, m.p. 136$^\circ$, gave a signal at $\delta$ 5.95s, integrating for 1 proton. This was assigned to a vinylic proton (C6-H) as in the epoxide (CCXVIII), no other vinylic proton was indicated. Further an unresolved multiplet centred at $\delta$ 3.38 integrating for 2 protons was ascribable to C3 and C4-protons. The narrowness of the peak ($\frac{1}{2}$ Hz $\sim$ 5 Hz) shows small coupling which indicates that the C3-H is equatorial (O) and that C4-H though axial (O) has small coupling with C3-H (equatorial proton) only. From this it is obvious that the epoxide oxygen (C3-C4) must be $\alpha$-oriented. This is in line with the general observation that the reagents prefer to attack a steroidal molecule from less hindered $\alpha$-side$^{144}$. 

![Diagram of chemical structures](image)
The n.m.r. spectrum of the \( \epsilon \)-lactones (CCXXI) or (CCXXII) will give signals for 3 vinylic protons. Further in structure (CCXXII) C8 proton will appear as a doublet of doublets at about \( \delta 4.2 \). From the consideration of above spectral properties it is reasonable to assign the epoxide structure (CCXVIII) to the compound, m.p. 136°.

The compound, (CCXIX), m.p. 205°, analysed correctly for \( \text{C}_{27}\text{H}_{44}\text{O}_3 \) and its mass spectrum gave molecular ion peak at m/e 416 (\( \text{C}_{27}\text{H}_{44}\text{O}_3 \)). From the elemental composition it is indicated that (CCXIX) may be the product of hydrolysis of the epoxide (CCXVIII; \( \text{C}_{27}\text{H}_{42}\text{O}_2 + \text{H}_2\text{O} \)). This indeed is the case, as has been shown by the conversion of (CCXVIII) into (CCXIX) by mild hydrolysis. The u.v. spectrum of the diol (CCXIX) (\( \lambda \) max. 244 nm; log \( \varepsilon \) 3.36) showed the presence of an \( \alpha , \beta \)-unsaturated ketonic group. Its i.r. spectrum showed peaks at 3360 (OH), 1680 (C=\( \text{C}-\text{C}=\text{O} \)), 1640 (sh) (C=C), 1075, 1022 and 1015 cm\(^{-1} \) (C-O).

The n.m.r. spectrum of (CCXIX) showed a sharp singlet at \( \delta 5.75 \) integrating for 1 proton and was assigned to C6-vinyllo proton. An unresolved multiplet centred at \( \delta 4.05 \) integrating for 2 protons was ascribable to C3 and C4 protons. The magnitude of splitting of this peak (\( \Delta \frac{1}{2} = 5 \text{ Hz} \)) showed that both the protons are equatorial (C3e- and C4e-), thus indicating that C3- and C4-hydroxy groups are axial (C3o(-OH and C4o(-OH). From mechanistic considerations it is to be expected that the epoxide ring will
open during hydrolysis to give trans diaxial diol such as

\((\text{CCXVIII}) \rightarrow (\text{CCXIX})^{144}\).

Though not very pertinent, a cursory comparison of the
n.m.r. spectrum of (CCXIX) was made with those of 5α-cholestane-
3β,6α-diol (CCXXIII) and 5α-cholestane-3β,6β-diol (CCXXIV) from
the chemical shift point of view of H-C-OH protons. In (CCXXIII)
both the protons (C3α- and C6β-protons) being axial appeared as
a broad peak centred at δ3.3. In (CCXXIV), C3α-H being axial
appeared as a broad peak centred at δ3.66 whereas C6β-H being
equatorial appeared as a relatively 'narrow' multiplet centred
at δ3.76 (lower field).

As expected, the diol (CCXIX) with acetic anhydride and
pyridine was converted into the diacetate, 3α,4β-diacetoxy-
cholest-5-en-7-one (CCXX). The diacetate (CCXX) in its mass
spectrum gave molecular ion peak at m/e 500 and analysed correctly
for C31H48O5. Its u.v. spectrum, as expected, showed absorption
maxima at 241 nm (log ε 3.63), supporting the α,β-unsaturated
carbonyl chromophore. The i.r. spectrum of (CCXX) showed peaks
at 1755(sh), 1740 (ester carbonyl), 1680 (C=C-CO−), 1640(sh)
(C=C−) and 1235 cm⁻¹ (acetate). The n.m.r. spectrum of (CCXX)
gave a singlet (1 proton) at δ5.9 ascribable to C6-vinyllic
proton. The C3 and C4 proton signals were well separated and
not merged together as in the case of diol (CCXIX). A doublet
(J = 3 Hz) at $\delta 5.22$ was assigned to $C4\alpha-H$ (equatorial) and a broader peak at $\delta 4.96$ was assigned to $C3\beta-H$ (equatorial), since $C3$ proton interacts with $C2$-methylene and $C4$-methine protons (3 protons interaction compared with 1 proton interaction of $C4-H$). The presence of two acetate groups was revealed by two sharp singlets at $\delta 2.05$ and $2.02$ (3 protons each).

Chemical shifts of $C3$ and $C4$ protons of (CCXX) were compared with those of $C3$ and $C6$ protons of the diacetates $5\alpha$-cholestan-3$\beta$,6$\alpha$-diol diacetate (CCXXV) and $5\alpha$-cholestan-3$\beta$,6$\beta$-diol diacetate (CCXXVI). In (CCXXV) both $C3$ and $C6$ protons being axial appeared as a broad multiplet centred at $\delta 4.64$. On the other hand in (CCXXVI) $C3\alpha-H$ being axial appeared as a broad peak centred at $\delta 4.7$ whereas, $C6\alpha-H$ being equatorial appeared as a relatively 'narrow' peak centred at $\delta 4.9$ (lower field).
The effect of different substituents at C3 and C4 as in (CCXVIII), (CCXIX) and (CCXX) on the C19-H signal is obvious. The ClO-methyl signals appeared at δ1.08, 1.34 and 1.31 in (CCXVIII), (CCXIX) and (CCXX), respectively.

The mass spectrum of 3α,4α-epoxycholest-5-en-7-one (CCXVIII) (Fig. 3) showed strong molecular ion peak at m/e 398 (base peak), with other salient peaks at m/e 383 (M-CH3), m/e 380 (M-H2O), m/e 370 (M-CO), m/e 285 (M-C8H17 side chain), m/e 203 (C13H15O2), m/e 190 (C12H14O2), m/e 177 (C11H13O2) and m/e 150 (C9H10O2).

The spectrum of (CCXVIII) can easily be related with that of the starting dienone (CCXVII)\(^{147}\). The presence of 3α,4α-epoxy group does not seem to make notable difference on the fragmentation pattern. The formation of fragment ions m/e 285, m/e 203, m/e 190, m/e 177 and m/e 150 can be shown as for the ions m/e 269, m/e 187, m/e 174, m/e 161 and m/e 134, respectively in the mass spectrum of the dienone (CCXVII) and can be formulated as shown below:
It is pertinent to point out that in the mass spectrum of the epoxide (CCXVIII) peaks at m/e 382, m/e 187, m/e 174 and m/e 161, typical of the dienone (CCXVII) were also observed. All the standard care was taken in the purification of the epoxide (CCXVIII) and its n.m.r. and i.r. spectra do not show the presence of the dienone (CCXVII). It is therefore reasonable to suggest that under electron impact the epoxy oxygen is eliminated to give the dienone species which undergoes fragmentation in the usual manner. However, this suggestion should be considered with caution as trace amounts of dienone (CCXVII) present as impurity in the epoxide (CCXVIII) can not be completely ruled out.

The presence of two vicinal hydroxy 1 groups in 3α,4β-dihydroxycholest-5-en-7-one (CCXIX) (Fig. 4) makes the spectrum a bit more complicated than that of (CCXVIII). However, comparable peaks are observed in the spectrum of (CCXIX) and their rationalization is possible relative to (CCXVIII). The mass spectrum of (CCXIX) showed a strong molecular ion peak at m/e 416 (base peak; C_{27}H_{44}O_{3}); other salient peaks were observed at m/e 401 (M-CH_{3}),
m/e 398 ($M-H_2O$), m/e 383 ($M-H_2O + CH_3$), m/e 370 ($M-H_2O + CO$), m/e 303 ($M-C_9H_{17}$ side chain), m/e 285 ($M-H_2O + C_8H_{17}$), m/e 208 ($C_{12}H_{16}O_3$), m/e 190 ($C_{12}H_{14}O_2$), m/e 177 and m/e 150.

Precise formulation of the ion m/e 398 ($M-H_2O$) is difficult in the absence of mass spectra of appropriate deuterated analogues of (CCXIX). The loss of water molecule from the molecular ion may involve 1,3-elimination ($C_3\alpha-OH$ and $C_1-H/C_4\beta-OH$ and $C_2-H$) as well as 1,4-elimination involving $C_4\beta-OH$ and $C_1-H$ as in the case of elimination of water molecule from cyclohexanol. It may be assumed that in the presence of a conjugated system such as in (CCXIX), the loss of water molecule may involve 1,2-elimination (say for example $C_3\alpha-OH$ and $C_4\alpha-H$) to give a stable system tentatively suggested as (a).

![Diagram](image)

(CCLXII)  
\[ m/e \ 398 \]

The fragment ion m/e 208 ($C_{12}H_{16}O_3$) may be formulated as (b) and the loss of a molecule of water from this will give the ion (c) m/e 190 ($C_{12}H_{14}O_2$).
Other fragment ions such as m/e 177 and m/e 150 may be formulated as (d) and (e) respectively.

The mass spectrum of 3α,4β-diacetoxycholest-5-en-7-one (CCXXI) (Fig. 5) is much more complicated than that of (CCXVIII). The mass spectrum shows a very weak molecular ion peak at m/e 500 (C_{31}H_{48}O_{5}), the other salient peaks are at m/e 440 (M-CH_3COOH), m/e 398 (440-CH_2=CH=0; C_{27}H_{42}O_2), m/e 396 (440-CO_2; C_{28}H_{44}O), m/e 383 (398-CH_3); m/e 381 (396-CH_3), m/e 380 (398-H_2O), m/e 370 (398-CO), m/e 327 (440-C_8H_{17} side chain), m/e 232 (C_{14}H_{16}O_3), and m/e 188 (C_{13}H_{16}O).
The loss of acetic acid is typical of acetates and this loss occurs predominantly by 1,2-elimination. From (CCXX) the loss of a molecule of acetic acid may involve \(3\alpha\)-acetate + \(4\alpha\)-H or/and \(4\beta\)-acetate + \(3\beta\)-H. In either case a double bond between C3-C4 will be created thus extending the conjugation. The third possibility involving \(3\alpha\)-acetate and C2-H may also be considered.

\[
\begin{align*}
\text{(CCXX)} & \\
\text{AcO} & \text{OAc} & \text{C}_{8}H_{17} \quad \text{AcO} & \text{OAc} & \text{AcO} & \text{OAc} \\
-\text{CH}_3\text{COOH} & & & & & \\

\text{(f)} & \quad \text{(g)} & \quad \text{(h)}
\end{align*}
\]
For the present discussion, ion (f) has been arbitrarily chosen to explain the breakdown pattern (though ion g could be used with equal effectiveness for this purpose. Ion h has not been given much consideration as conjugated systems like f or g is more likely to dominate). The fragment ion m/e 440 (M-\text{CH}_3\text{COOH}) does not show further loss of acetic acid and there appears to be no rationale for such a loss, instead, a molecule of CO_2 is lost to give the fragment ion m/e 396 (C_{28}H_{44}O). Ion f has been used in the following schemes to show the formation of salient peaks.

m/e 398

From the composition (C_{27}H_{42}O_2) it appears that it is derived from the ion m/e 440 by the loss of a molecule of ketene^{147}. This assumption was supported by a metastable peak at 360.

\[ \text{m/e 440} \]
\[ \text{(f)} \]
\[ \text{m/e 398 (C}_{27}\text{H}_{42}\text{O}_2) \]
m/e 396

The composition C_{28}H_{44}O suggests that a molecule of CO$_2$ is lost from the ion 440 to give the fragment ion m/e 396.

Fragment ions m/e 232 and m/e 188 from (CCXX) have been formulated as (k) and (l), respectively.
Reaction of cholesta-3,5-dien-7-one (CCXVII) with performic acid.

As mentioned earlier the reaction of cholesta-3,5-dien-7-one (CCXVII) with perbenzoic acid provided 3α,4α-epoxycholesta-5-en-7-one (CCXVIII) and its artefact, 3α,4β-dihydroxycholesta-5-en-7-one (CCXIX) and none of the expected β-lactones, 7α-oxa-B-homocholesta-3,5-dien-7-one (CCXXI) and 7-oxa-B-homocholesta-3,5-dien-7α-one (CCXXI) or the products derived from them was obtained.

\[ \text{(CCXVII)} \quad \text{(CCXXI)} \quad \text{(CCXXII)} \]

In order to obtain the β-lactones (CCXXI) and (CCXXII), the dienone (CCXVII) was treated with the varying quantities of performic acid for different lengths of time. Invariably, this reaction, after usual workup and column chromatography provided the epoxide (CCXVIII), the diol (CCXIX), 3α-formyloxy-4β-hydroxycholesta-5-en-7-one (CCXXVII), m.p. 162°, and cholesta-5-ene-3,7-dione (CCXXX), m.p. 165°; the relative amounts of these products
depended largely upon the experimental conditions. The homogeneity of these products was ensured by t.l.c. using different solvent systems.

Characterization of the compound, m.p. 162° as 3α-
formyloxy-4β-hydroxycholest-5-en-7-one (CCXXVII).

The compound, m.p. 162° analysed correctly for C_{28}H_{44}O_{4}.
From the elemental composition it is evident that 3 oxygen atoms have been introduced during the reaction. The i.r. spectrum of the compound, m.p. 162° gave peaks at 3455(OH), 1735(-C=O-), 1685 (-C=C-), 1620 (C=C), 1185 (formate ester), 1075 and 1020 cm⁻¹ (C-O⁻). The presence of an α,β-unsaturated carbonyl group was further substantiated by the u.v. spectrum of the compound (λ max. 242 nm, log ε 3.48).

To accommodate the above i.r. spectral values two possible structures (CCXXVII) and (CCXXVIII) for the compound, m.p. 162° could be suggested which can possibly arise from the reaction conditions.

(CCXXVII)  
(CCXXVIII)
The n.m.r. spectrum of the compound, m.p. 162° gave signals at \( \delta 8.1 \) s (1 proton, \(-O-C-H\)), \( \delta 5.3 \) s (1 proton, \( C6-H \), vinylic proton), \( \delta 5.26 \) br (1 proton, \( \frac{1}{2} 8 \) Hz, \( HC3-O-C-\), equatorial, \( \beta \)-oriented), \( \delta 4.6 \) br s(C4-OH, disappeared on addition of \( D_2O \)), \( \delta 4.2 \) d like (1 proton, \( J=3.5 \) Hz; \( \frac{1}{2} 5 \) Hz, \( H-C4-OH \), equatorial, \( \alpha \)-oriented), \( \delta 1.4 \) s (3 protons, \( C10-Me \)), \( \delta 0.7 \) s (3 protons, \( C13-Me \)), \( \delta 0.93 \) and \( \delta 0.85 \) (other methyl signals). On addition of \( D_2O \), only the signal at \( \delta 4.6 \) disappeared and there was no significant change in any other part of the spectrum. The chemical shifts and magnitude of splitting for C3 and C4 protons clearly indicated that both of them are equatorially oriented. The downfield signal at \( \delta 5.26 \) should be ascribed to a proton attached to the carbon carrying the formate group, and the one at \( \delta 4.2 \) should be ascribable to the proton attached to the carbon carrying a hydroxyl group. From the shape and magnitude of splitting of the signal at \( \delta 5.26 \), it is evident that this one is interacting with at least 3 vicinal protons, whereas the signal at \( \delta 4.26 \) (doublet like) is interacting with one proton, as in the structure (CCXXVII). In the alternate structure, one would expect the broader signal to be at the relatively higher field (\( H-C3-OH \)), say at about \( \delta 4.2 \); and the downfield signal at \( \delta 5.26 \) to be narrower and doublet like. On the basis of n.m.r. spectrum, the compound, m.p. 162° has been assigned the structure (CCXXVII).
This was further supported by the fact that the formate (CCXXVII) on mild hydrolysis, as expected provided the diol (CCXIX); though it must be pointed out that the alternate structure (CCXXXVIII) would have given the same diol (CCXIX) on hydrolysis.

It is worthwhile to comment on the mode of the formation of the formate (CCXXVII) in this reaction. The epoxides (in rigid cyclic system, say cyclohexane in the chair conformation) normally open to furnish diaxially oriented functionalities. If it be assumed that the $\alpha$-epoxide (CCXVIII) is involved as the precursor, then from mechanistic consideration one should get $3\alpha$-hydroxy-$4\beta$-formyloxycholest-5-en-7-one (CCXXXVIII) as the product of formolysis and not $3\alpha$-formyloxy-$4\beta$-hydroxycholest-5-en-7-one (CCXXVII) as shown in the following scheme. (Although some deformation of ring A is possible because of C5-C6 double bond).

![Diagram](https://via.placeholder.com/150)

(CCXVIII)

(CCXXXVIII)
The epoxide (CCXVIII) does indeed open to give the diaxially oriented dihydroxy compound (CCXIX) on mild hydrolysis. However, as argued earlier, the n.m.r. values support the structure (CCXXVII). Alternatively it is reasonable to believe that the precursor of 3$\alpha$-formate compound (CCXXVII) is the diol (CCXIX) which is formed during the course of the reaction and undergoes selective esterification of the C3-OH group. In the diol (CCXIX) both the C3, and C4-hydroxyl groups are axial and therefore should show reluctance to ready esterification because of 1,3-diaxial interaction. However, the axial OH at C4 ($\beta$-oriented) would be more affected because of its interaction with C10-methyl group (severe interaction), and C2-axial hydrogen and therefore, would be less accessible for esterification in comparison to C3-OH ($\alpha$-oriented, axial) which would have interaction with only C1-axial hydrogen. This could account for the preferential esterification of C3-OH.

![Chemical structures](image)
Characterization of the compound, m.p. 165° as cholest-
5-ene-3,7-dione (CCXXX).

The compound, m.p. 165° analysed correctly for C₂₇H₄₂O₂. From the elemental composition it is apparent that only one oxygen has been incorporated during the course of the reaction. The i.r. spectrum gave peaks at 1705 (C=O), 1680 (C=C=C-) and 1625 cm⁻¹ (C=C). Its u.v. spectrum showed absorption maxima at 242 nm (log ε 3.65) thus further supporting the presence of an α,β-unsaturated carbonyl chromophore. The n.m.r. spectrum gave signals at 6 6.15 (1 proton; C₆-H, vinylic proton), 2.15 umc (4 protons, C₂-H₂ and C₄-H₂), 1.2 (C₁₀-Me), 0.71 (C₁₃-Me), 0.95 and 0.85 (other methyl signals); there was no other signal in the region 6 2.5-10 (except the one at 6 6.1 as mentioned above). From the elemental composition and spectral data, it is clear that this compound (m.p. 165°) is none of the expected lactones (CCXXI) and (CCXXII). The i.r. spectrum clearly showed the presence of two carbonyl functions (1705 for saturated ketone, and 1680 cm⁻¹ for an α,β-unsaturated ketone). Two enediones (CCXXIX) and (CCXXX) can result from the acid-catalysed isomerization of the intermediate epoxide (CCXVIII).
The i.r., n.m.r. and u.v. spectral values support the structure (CCXXX) i.e. the compound under discussion is cholest-5-ene-3, 7-dione (CCXXX) and not cholest-5-ene-4,7-dione (CCXXIX). It is reasonable to assume that a small amount of cholest-4-ene-3, 7-dione (CCXXXa) may also be present in equilibrium.