Part One

A. Sulfur Derivatives of Steroids
Theoretical

The condensation of ethanedithiol with steroidal and non steroidal ketones is a well known method for the formation of cyclic products as well as for the protection of the ketones under different reaction conditions\(^1,2\). Due to their ease of formation and chemical stability, these compounds are regarded as intermediates in multistage synthesis\(^3\).

Dithiolanes have become of interest in recent years on account of their pharmacological potentialities\(^4\). Some dithiolanes have been identified as components of anal gland secretion of the ferret\(^5\). Isoprothiolanes and other related compounds have been studied for the systematic control of rice blast caused by *Pyricularia oryzae* and planthoppers\(^6\). A few steroidal dithiolanes were also reported for modest activity in seroflocculation reaction with cancer sera\(^7\). A recent report has described the dithiolanes and oxathiolanes as radio protectant\(^8\).

The number of known organic sulfur compounds are very large and their chemistry in some respect is more complicated than that of oxygenated compounds. Thioethers can be expected
to be a convenient intermediates in the preparation of individual sulfur derivatives of steroids. Thioethers are prepared by the direct addition of sulfur or sulfur compounds to double bond of unsaturated compounds. These thioethers possess biological and industrial value. They have been used in the preparation of thermo and photostable polyamides, in increasing the thermal stability of rubber and polymers. Steroidal thioethers were used to assay steroidal hormones, using radioimmunoassay techniques. Recently some thioethers were tested for antiinflammatory, bactericidal, fungicidal, anticholesteremic and hypolipemic activities. Few thioethers were also tested as tranquilizers.

Thioketals, hemithioketals and thioethers are oxidizable to the corresponding sulfoxides and sulfones. The utility of these sulfoxides and sulfones are limited due to their unstability towards the alkaline reagents. Sulfones are reported to possess antitubercular, antitumor and antiinflammatory activities. They are used as herbicides, as wetting, and as emulsifying agents. Some other sulfones of diphenyl derivatives are also used as plant growth regulator.
A. Steroidal dithiolanes

Hauptmann studied the behavior of different mercaptans with steroidal ketones in the presence of \( \text{Na}_2\text{SO}_4 \), \( \text{ZnCl}_2 \) or \( \text{HCl} \) gas. He reported that ethanedithiol condensed readily with keto group at the carbon atoms 3,7,12 and 17 of the steroidal skeleton.

\[
\begin{align*}
\text{(I)} & \quad \text{C}_{30}\text{H}_{51}\text{SH} \\
\text{[SH, ZnCl}_2 \quad \text{Na}_2\text{SO}_4] & \quad \text{C}_{30}\text{H}_{51}\text{S}_2
\end{align*}
\]

Ralls et al. treated 3\( \beta \)-acetoxycholest-5-en-7-one (III) with mercaptan and reported that the formation of corresponding mercaptol did not occur readily, but when it was treated with ethanedithiol in presence of absolute ether and hydrogen chloride, the thioketal (IV) was obtained in good yield.
Sheehan et al.\textsuperscript{31} reported the reaction of 1,3-propane-dithiol with 16-keto-17\(\beta\)-estradiol-17-acetate-3-methyl ether (V) in presence of ZnCl\(_2\) and HCl which furnished the thio-ketal (VI) in good yield.
Djerassi and coworkers\textsuperscript{32} reported that if keto groups are present at 11- and 12-positions of the steroid skeleton, only 12-ketone undergoes condensation. They obtained 22a, 5\(\alpha\)-spirostan-3\(\beta\)-ol-11,12-dione 12-ethylene thioketal (VIII) from 22a, 5\(\alpha\)-spirostan-3\(\beta\)-ol-11,12-dione (VII) using ethanedithiol and anhydrous HCl gas.

\[ \text{(VII)} \quad \rightarrow \quad \text{(VIII)} \]

Fieser\textsuperscript{2} treated \(\Delta^4\)-cholesten-3,6-dione (IX) with ethanedithiol using BF\(_3\)-etherate as a catalyst and obtained thioketal (X). He also prepared some other steroidal thioketals by the same method and reported that the addition of BF\(_3\)-etherate to the acetic acid solution of ketones (XI,XIII) and excess of ethanedithiol yielded the corresponding thioketals (XII,XIV) promptly.
Stevenson and Fieser\textsuperscript{33} reported the formation of dithiolanes XV\textsubscript{IX} and XVI from the ketones XVII, XVIII and XV respectively.

\[ \text{XV} \rightarrow \text{XVI} \]

\[ \begin{align*}
&\text{(XV)} \\
\text{SH} &\text{SH} \\
\text{(XVI)} 
\end{align*} \]
Fieser and Stevenson\textsuperscript{34} reported the involvement of some allylic rearrangement during the condensation of ethanedithiol with ketone(XX), catalyzed by BF\textsubscript{3}-etherate. They reported the formation of cholestan-3,6-dione bis-ethylene dithiolane (XII) from $\Delta^5$-cholesten-4\textalpha-ol-3-one acetate (XX).

![Chemical structure](image)

Pappas and Nace\textsuperscript{35} reported that the ethanedithiol is superior to ethylene glycol as a blocking agent for 20-keto function as shown in the conversion of 2-carbomethoxy-A-norallolopregnan-20-one(XXI) into 2-methylal derivative (XXIII).

![Chemical structure](image)
Blickenstaff and Foster\textsuperscript{7} converted testosterone acetate (XXIV) and 3\(\beta\)-chloro-5-androsten-17-one (XXVI) to their respective thioketals (XXV, XXVII) by the reaction of ethanedithiol.

\[
\begin{align*}
\text{(XXIV)} & \xrightarrow{\text{SH, SH}} \text{(XXV)} \\
\text{(XXVI)} & \xrightarrow{\text{SH, SH}} \text{(XXVII)}
\end{align*}
\]
Ralls and Riegel\textsuperscript{3} studied the reaction of ethanedithiol under mild conditions with ketones (XXVIII), (XXIX) and (XXXII) and reported that reaction took place primarily at 3-position in each case.

\[
\text{RSH, AcOH} \xrightarrow{\text{p-Toluenesulfonic acid}} \text{S-S}
\]

\[
R \quad \text{(XXVIII)} \quad \text{OH} \quad (XXX) \quad \text{OH}
\]

\[
R \quad \text{(XXIX)} \quad \text{H} \quad (XXXI) \quad \text{H}
\]

\[
(XXXII) \quad \rightarrow \quad (XXXIII)
\]
Fieser and coworkers subjected ketones (XXXIV) and (XXXV) to the reaction with ethanedithiol and obtained thioketals (XII) and (XXXVI), (XXXVII) respectively.

(XXXIV) \[ \rightarrow \] (XII)

(XXXV) \[ \rightarrow \] (XXXVI) + (XXXVII)
Kupchan et al.\textsuperscript{37} prepared ethylenethioketal (XXXIX) and bis-ethylenethioketal (XLI) by the reaction of $5\alpha$-cholestan-4$\alpha$-ol-3-one-4-acetate (XXXVIII) and cholestan-4$\alpha$-ol-3,7-dione-4-acetate (XL) with ethanedithiol and BF$_3$-etherate. Weiss et al.\textsuperscript{38} reported the synthesis of (XLII) which has shown variety of biological activities.
Pettit et al.\textsuperscript{39} treated (XLIII) with ethanedithiol in the presence of HClO\textsubscript{4} at 25\textdegree to give the corresponding thioketal (XLIV). Williams and Sarkisian\textsuperscript{40} prepared mono-thioketals (XXXI) and (XLVI) from diketones (XXIX) and (XLV) respectively.
Akhrem et al.\textsuperscript{41} prepared 12-thioketal of 8-aza-16-oxagonan-12,17-dione derivative (XLVIII) by the reaction of dione (XLVII) with ethanedithiol in acidic medium. This thioketal has been used as intermediate in the synthesis of biologically active 8-aza-16-oxagonane derivatives.
B. **Desulfurization of steroidal dithiolanes with Raney nickel**

Hydrogenolytic desulfurization with Raney nickel is a very useful tool in organic synthesis. It became an everyday procedure for the removal of sulfur from its derivatives.\(^{42-46}\) The removal of sulfur by Raney nickel follows a free radical mechanism. The desulfurization with Raney nickel has been used for several organic structural and other synthetic problems.

\[
\begin{array}{c}
\text{R} \\
\text{S} \\
\text{C} \\
\text{S} \\
\text{R'}
\end{array} \rightarrow \begin{array}{c}
\text{R} \\
\text{CH}_2 \\
\text{R}
\end{array}
\]

Wolfrom and Karabinos\(^{47}\) have reported this method for transferring the mercaptols of aliphatic and aromatic ketones into corresponding sulfur free derivatives. This method for the transformation of carbonyl group into methylene group is superior to the other methods.\(^{1,48,49}\) Several thioethers and dithioketals in steroid series have been transformed into sulfur free compounds. In a few cases, where double bond was present, the deactivated Raney nickel was used, due to which the double bond remained unaffected. Hauptmann\(^{50}\) applied this method for the desulfurization of thio-ketal of
cholest-4-en-3-one into cholest-4-ene. The different steroidal dithioketals have been desulfurized with Raney nickel to yield the corresponding sulfur free compounds. Some of them are given in Table - I.

Table - I

<table>
<thead>
<tr>
<th>Starting Compound</th>
<th>Product</th>
<th>Yield %</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AcO</td>
<td>AcO</td>
<td>62</td>
<td>51</td>
</tr>
<tr>
<td>COOCH₃</td>
<td>COOCH₃</td>
<td>65</td>
<td>52</td>
</tr>
<tr>
<td>CH₃O</td>
<td>COOCH₃</td>
<td>95</td>
<td>53</td>
</tr>
</tbody>
</table>

![Structural diagrams of compounds]

- **AcO** refers to acetyl group.
- **COOCH₃** refers to acetate ester group.
- **CH₃O** refers to methoxy group.
- **OH** refers to hydroxyl group.
Table - I (Contd.)

<table>
<thead>
<tr>
<th>Starting Compound</th>
<th>Product</th>
<th>Yield %</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Start Compound 1" /></td>
<td><img src="image2" alt="Product 1" /></td>
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<td>33</td>
</tr>
<tr>
<td><img src="image3" alt="Start Compound 2" /></td>
<td><img src="image4" alt="Product 2" /></td>
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<td>36</td>
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<tr>
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<td><img src="image6" alt="Product 3" /></td>
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Table - I (Contd.)

<table>
<thead>
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<th>Product</th>
<th>Yield %</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
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<td><img src="image2.png" alt="Product 1" /></td>
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<td>1</td>
</tr>
<tr>
<td><img src="image3.png" alt="Starting Compound 2" /></td>
<td><img src="image4.png" alt="Product 2" /></td>
<td>36</td>
<td>54</td>
</tr>
<tr>
<td><img src="image5.png" alt="Starting Compound 3" /></td>
<td><img src="image6.png" alt="Product 3" /></td>
<td>74</td>
<td>36</td>
</tr>
</tbody>
</table>
When the dithioketal having carbonyl group neighbouring to the sulfur bearing carbon atom was subjected to desulfurization, the carbonyl group was unaffected but acetoxy group neighbouring to the sulfur bearing carbon atom was mostly affected, as given in Table - II.

Table - II

<table>
<thead>
<tr>
<th>Starting Compound</th>
<th>Product</th>
<th>Yield %</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>44</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80</td>
<td>55</td>
</tr>
</tbody>
</table>
Table - II (Contd.)

<table>
<thead>
<tr>
<th>Starting Compound</th>
<th>Product</th>
<th>Yield %</th>
<th>Ref.</th>
</tr>
</thead>
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<td><img src="image1.png" alt="Chemical Structure" /></td>
<td><img src="image2.png" alt="Chemical Structure" /></td>
<td>78</td>
<td>56</td>
</tr>
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<td><img src="image3.png" alt="Chemical Structure" /></td>
<td><img src="image4.png" alt="Chemical Structure" /></td>
<td>50</td>
<td>37</td>
</tr>
</tbody>
</table>

The nature of the reaction product in desulfurization mostly depends on the activity of Raney nickel. When the thioketal (XLIX) was refluxed with Raney nickel, the saturated product (L) was obtained but in case of less active Raney nickel the double bond remained intact after desulfurization\(^57\).
C. Steroidal sulfoxides and sulfones

The sulfoxides and sulfones have been prepared by the treatment of thioketals with different oxidizing agents like $\text{KMnO}_4$, $\text{H}_2\text{O}_2$, peroxytrifluoroacetic acid and meta-chloroperbenzoic acid. Romo et al. prepared 3- and 16-sulfoxides (LII, LIV) by the action of $\text{H}_2\text{O}_2$ in dioxane.
Djerassi and Engle treated steroidal hemithioketal (LV) with ruthenium tetraoxide in carbon tetrachloride and reported the formation of sulfone (LVI). The same sulfone (LVI) was obtained when steroidal hemithioketal (LV) was treated with monoperphthalic acid, but with 30% H₂O₂, sulfoxide (LVII) was reported as product. 

\[ \text{Ruthenium tetraoxide} \quad \text{CCl}_4 \quad \text{H}_2\text{O}_2 \] 

\[ \text{SCH}_2\text{C}_6\text{H}_5 \quad \text{SOCH}_2\text{C}_6\text{H}_5 \] 

\[ \text{(LIII)} \quad \text{(LIV)} \]
Heaton et al.\textsuperscript{62} reported the oxidation of thioketals (LVIII) and (LXI) with I-chlorobenzotriazole, the sulfoxides (LX, LXIII) and sulfones (LIX, LXII) were obtained.
Vesely et al.\textsuperscript{63} treated the 17\(\beta\)-acetoxy-3,3-ethylene-dithioandrost-4-ene (XXV) with hydrogen peroxide in acetic acid and obtained the corresponding disulfones (LXIV) and ethylenesulfinylsulfonyl derivative (LXV) as a side product.

\[
\begin{align*}
&\text{(XXV)} & \text{(LXIV)} & \text{(LXV)} \\
\end{align*}
\]

Daum and Clark\textsuperscript{22} prepared the 3,3-ethylenedisulfonyl-5\(\alpha\)-androstan-17\(\beta\)-ol acetate (LXVII) by the reaction of thioketal (LXVI) with an excess of monoperphthalic acid in ether and tetrahydrofuran solution. Sulfone (LXIX) was obtained by the oxidation of (LXVIII) with m-chloroperbenzoic acid\textsuperscript{26}.

\[
\begin{align*}
&\text{(LXVI)} & \text{(LXVII)} \\
\end{align*}
\]
D. Steroidal thioethers

Ralls and coworkers\(^3\) prepared the thioethers from \(\alpha,\beta\)-unsaturated steroidal ketones. They treated 3\(\beta\)-acetoxycholest-5-en-7-one (III), its 3\(\beta\)-chloro analogue (LXX) and 3,5-cholestadien-7-one (LXXI) with ethyl mercaptan in the presence of acetic acid and hydrochloric acid to obtain 3-ethylthio-5-cholesten-7-one (LXXII).
Rosenkranz et al. prepared steroidal thioethers (LIX, LXXXIII, LXXXIV) by the reaction of benzyl or ethyl mercaptan with α,β-unsaturated ketones (XXIX, I) in the presence of different catalytic agents.
Kaneko et al. treated 17α-acetoxypregna-4,6-dien-3,20-dione with RSH (R = alkyl or aryl) and obtained the corresponding 17α-acetoxy-7α-[alkyl (or aryl) thio]-pregn-4-en-3,20-dione (LXXV) which was found useful as a corpus luteum hormone.
Romo et al. treated 2-mercaptoethanol in the presence of piperidine with \( \Delta^{5,16} \)-pregnadien-3\( \beta \)-ol-20-one-3-acetate (LXXVI) and \( \Delta^{4,16} \)-pregnadien-3,20-dione (LXXVIII) and obtained the corresponding thioethers (LXXVII) and (LXXIX).

Takeda et al. treated 6\( \beta \)-bromo-4-en-3-one steroid (LXXX) with CH\(_2\)COSK, which yielded the corresponding 6\( \alpha \)-acetyltio-4-en-3-one (LXXXI).
Yamato and coworkers prepared thioethers (LXXV) which were tested for progestational activity in rabbits. Eliassaf reported the synthesis of LXXXII.

\begin{align*}
\text{(LXXV)} & \\
\text{(LXXXI)} & \\
R = \text{alkyl or aryl}
\end{align*}
Miyake and Tomoedo\textsuperscript{69} reported the preparation of $6\beta$-hydroxy-4-(\(\beta\)-hydroxyethylthio-)cholest-4-en-3-one (LXXXIV) by the photooxidation of cholesta-3,5-dieno[3,4-\(b\)]-1,4-oxathiane (LXXXIII). The thioether (LXXXV) has also been prepared and found useful in the treatment of eye and skin diseases.
Kaneko et al. prepared 7α-benzylthio or ethylthio-compound (LXXXVII) by the reaction of 17β-hydroxy-17α-methylandrosta-4,6-dien-3-one (LXXXVI) with \( C_6H_5CH_2SH \) or aryl mercaptan in dioxane. Lee et al. prepared cholesteryl and isocholesteryl thioethers (LXXXIX, XC) by the solvolysis of cholesterol tosylate (LXXXVIII) in the presence of RH.

\[
\text{(LXXXVI)} \quad \xrightarrow{\text{Solvolysis RH}} \quad \text{(LXXXVII)}
\]

\[
\text{(LXXXVIII)} \quad \xrightarrow{\text{Solvolysis RH}} \quad \text{(LXXXIX)} + \text{(XC)}
\]

\[
\begin{align*}
R & \quad \text{HOCH}_2\text{CH}_2\text{S}^- \\
& \quad \text{HSCH}_2\text{CH}_2\text{S}^- \\
& \quad \text{PhS}^-
\end{align*}
\]
Hosoda and coworkers\textsuperscript{72-76} reported that 4,5-epoxide of steroids when subjected to react with HS(CH\textsubscript{2})\textsuperscript{n}COOH (n = 1, 2), the steroidal thioethers (XCII) were obtained.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{diagram.png}
\caption{(XCII)}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{diagram.png}
\caption{(XCI)}
\end{figure}

Brueggemeier and coworkers\textsuperscript{77} reported 7α-(4′-amino) phenylthioandrost-4-en-3,17-dione (XCIII) as the most effective inhibitor of aromatase. The other derivatives of this thioether having the alkylating moieties were tested as irreversible enzyme inhibitors.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{diagram.png}
\caption{(XCIII)}
\end{figure}
Zwirner et al. treated androst-5-en-3β,17β-diol-3-acetate-17-benzoate (XCVI) with N-bromosuccinimide and \( \text{HSCH}_2\text{CH}_2\text{COOMe} \), followed by saponification to yield the carboxyethylthioesterone (XCV) which is a biologically active thioether.

\[
\text{AcO} \quad \text{OBz} \\
\text{1. NBS/HS(CH}_2\text{)_2COOMe} \\
\text{2. Saponification} \\
\text{HO} \\
\text{SCH}_2\text{CH}_2\text{COOH}
\]

(XCVI) (XCV)

Recently Husain et al. reported the synthesis of thioethers (XCVc) and (XCVd,e) by the reaction of 3-mercapto-propan-1,2-diol with fatty acid (XCVa) and ester (XCVb) respectively in the presence of acetic acid and BF₃-etherate as catalyst.

\[
\text{CH}_3\text{(CH}_2\text{)}_{14}\text{CH}=\text{CH-COOH} \quad \text{BF}_3\text{-etherate} \quad \text{CH}_3\text{(CH}_2\text{)}_{14}\text{CHCH}_2\text{COOH} \quad \text{SCH}_2\text{CHCH}_2\text{OAc} \\
\text{OH} \quad \text{OH} \quad \text{OH}
\]

(XCVa) (XCVc)

\[
\text{CH}_2=\text{CH-(CH}_2\text{)_8-COOCH}_3 \quad \text{CH}_2\text{(CH}_2\text{)}_9\text{COOCH}_3+\text{CH}_2\text{(CH}_2\text{)_6COOCH}_3 \\
\text{SCH}_2\text{CHCH}_2\text{OAc} \quad \text{SCH}_2\text{CHCH}_2\text{OAc} \quad \text{SCH}_2\text{CHCH}_2\text{OAc} \quad \text{OH}
\]

(XCVb) (XCVd) (XCVe)
Dithiolanes

Dithiolanes (thioketals) are readily formed by the condensation of 1,2-ethanedi-thiol with ketones under a variety of conditions. The importance of dithiolanes is mainly because of the biological activities related with them. Physiological values of these compounds prompted us to undertake the synthesis of steroidal dithiolanes. The easily accessible steroidal saturated as well as $\alpha,\beta$-unsaturated ketones, prepared according to the literature procedure were subjected to react with 1,2-ethanedi-thiol. Several steroidal dithiolanes were obtained and their structures were established on the basis of their spectral properties and chemical transformations.

Reaction of 5α-cholestan-6-one (XCVI) with 1,2-ethanedi-thiol

5α-Cholestan-6-one (XCVI) was allowed to react with 1,2-ethanedi-thiol in the presence of acetic acid and BF$_3$-etherate at room temperature$^2$. After completion of the reaction, the reaction mixture was worked up. Removal of
the solvents provided compound (XCVII) as a semi-solid.

Characterization of compound (XCVII) as 6,6-ethylenedithio-5α-cholestane

Elemental analysis of compound (XCVII) corresponded to formula $\text{C}_{29}\text{H}_{50}\text{S}_{2}$. Its IR spectrum showed no band for the carbonyl function which suggested the incorporation of dithiolane ring in the molecule. The important absorption bands appeared at 1430 and 1245 cm$^{-1}$ ($\text{H}_2\text{C-S}$). The NMR spectrum displayed singlet at δ 3.0 for four protons which was ascribable to dithiolane ring protons. Methyl protons appeared at δ 1.20 (Cl$\text{O-CH}_3$), 0.67 (Cl$\text{3-CH}_3$), 0.91 and 0.81 (other methyl protons). Thus on the basis of these data the compound (XCVII) was suggested to be 6,6-ethylenedithio-5α-cholestane.
The structure of compound (XCVII) was further supported by its desulfurization with Raney nickel, which yielded 5α-cholestane (XCVIII), m.p. 80-81° (reported m.p. 80°).

Oxidation of dithiolane (XCVII) with m-chloroperbenzoic acid

The dithiolane (XCVII) was treated with m-chloroperbenzoic acid in dichloromethane at 10°. TLC monitoring showed a complete conversion after 3 hr. Usual work up and purification by silica gel column afforded XCIX as a viscous liquid.

\[
\begin{align*}
\text{C}_8\text{H}_{17} & \quad \text{m-CPBA} \\
\text{CH}_2\text{Cl}_2 & \\
(\text{XCVII}) & \quad \Rightarrow \\
\text{OS} & \quad \text{SO} \\
\text{H} & \quad \text{H} \\
(\text{XCIX}) & 
\end{align*}
\]

Characterization of compound (XCIX) as 6,6-ethylenedisulfinyloxy-5α-cholestane

The microanalysis of compound XCIX corresponded to formula \( C_{29}H_{50}O_2S_2 \). The IR spectrum had a strong band at 1060 cm\(^{-1}\) which was characteristic to sulfoxide grouping. Its NMR spectrum exhibited a structure identifying signal at \( \delta 3.32 \) as a broad singlet for methylene protons (4H) \( \alpha \)-to sulfoxide groups. The lowering in chemical shift from \( \delta 3.0 \)
(in XCVII) to δ 3.2 is attributed to the conversion of sulfide to sulfoxide group. Methyl signals appeared at δ 1.23 (Cl0-CH₃), 0.73 (Cl3-CH₃), 0.93 and 0.83 (other methyl protons). On the basis of these data the viscous compound (XCIX) was characterized as 6,6-ethylenedisulfinyl-5α-cholestane.

**Reaction of 3β-acetoxy-5α-cholestan-6-one (C) with 1,2-ethanedithiol**

3β-Acetoxy-5α-cholestan-6-one (C) was treated with 1,2-ethanedithiol in acetic acid (BF₃-etherate as catalyst). After usual work up of reaction mixture and removal of the solvent, a compound (CI) having m.p. 149-151° was obtained in excellent yield.

Characterization of the compound, m.p. 149-151° as 3β-acetoxy-6,6-ethylenedithio-5α-cholestane (CI)

The compound m.p. 149-151° corresponded to molecular
formula $C_{31}H_{52}O_2S_2$. Its IR spectrum exhibited characteristic bands at 1747 (-OCOCH$_3$), 1435 and 1245 cm$^{-1}$ (CH$_2$-S). The NMR spectrum showed a broad multiplet centred at $\delta$ 4.7 (C3a-H, $\Delta^j = 14$Hz, axial$^{82a}$, a singlet at 3.18 ascribable to four protons (-S-CH$_2$CH$_2$-S-) of dithiolane ring and a three-proton singlet at 2.08 for acetoxy group protons. The methyl protons were seen at $\delta$ 1.18 (Cl0-CH$_3$), 0.68 (Cl3-CH$_3$), 0.90 and 0.80 (other methyl protons). Thus on the basis of above data the structure of compound having m.p. 149-151$^\circ$ was established as 3$\beta$-acetoxy-6,6-ethylenedithio-5$\alpha$-cholestane (CI).

Reaction of 3$\beta$-chloro-5$\alpha$-cholestan-6-one (CII) with 1,2-ethanedithiol

3$\beta$-Chloro-5$\alpha$-cholestan-6-one (CII) was allowed to react with 1,2-ethanedithiol in presence of acetic acid and BF$_3$-etherate at room temperature. On completion of reaction, the reaction mixture was worked up in the usual manner which gave a compound (CIII), m.p. 143$^\circ$. 

![Chemical structures](image-url)
Characterization of the compound, m.p. 143° as 3β-chloro-6,6-ethylenedithio-5α-cholestan (CIII)

The compound (CIII), m.p. 143° was analyzed for C_{29}H_{49}S_{2}Cl and gave positive Beilstein test. Its IR spectrum exhibited absorption bands at 1430, 1240 (H₂C-S⁻), 760 (C-Cl) and 675 cm⁻¹ (C-S). The NMR spectrum showed a singlet at δ 3.1 ascribable to four protons of dithiolane ring (-S-CH₂-CH₂-S-) and a broad multiplet centred at 3.9 (W½ = 16Hz; axial) for C3-α proton. Methyl protons were observed at δ 1.06 (C10-CH₃), 0.73 (C13-CH₃), 0.96 and 0.80 (other methyl protons). These spectral evidences suggested the structure of the compound melting at 143° as 3β-chloro-6,6-ethylenedithio-5α-cholestan (CIII).

The structure of dithiolane (CIII) was further confirmed by its desulfurization with Raney nickel which provided 3β-chloro-5α-cholestan (CIV), m.p. 113° (reported³³ m.p. 115°).

Reaction of 3β-bromo-5α-cholestan-6-one (CV) with 1,2-ethanedithiol

3β-Bromo-5α-cholestan-6-one (CV) was treated with 1,2-ethanedithiol in the same manner as described earlier. After usual work up of the reaction mixture, the compound having m.p. 139-140° was obtained in good yield.
Characterization of the compound, m.p. 139° as 3β-bromo-6,6-
ethylenedithio-5α-cholestane (CVI)

The compound (CVI), m.p. 139-140° was analyzed for
C_{29}H_{49}S_2Br and showed positive Beilstein test which suggested
the presence of bromine in the molecule. In the IR spectrum
characteristic absorption bands at 1435, 1240 (H_2C-S-),
680 (C-S) and 675 cm\(^{-1}\) (C-Br) were observed. Its NMR spectrum
displayed a broad multiplet for one proton at δ 3.9 (\(W_1 = 15\text{Hz}\))
which was assigned to C3-α H (axial) and a singlet at 3.11
integrating for four protons of dithiolane ring (-S-CH\(_2\)-CH\(_2\)-S-).
Methyl protons were seen at δ 0.93 (Cl0-CH\(_3\)), 0.63 (Cl3-CH\(_3\)),
0.86 and 0.78 (other methyl protons). These spectral data
confirmed the structure of the compound melting at 139-140°
as 3β-bromo-6,6-ethylenedithio-5α-cholestane (CVI).
Reaction of 3β-iodo-5α-cholestan-6-one (CVII) with 1,2-ethanedithiol

The ketone (CVII) was allowed to react with 1,2-ethanedithiol in the same manner as employed in the previous cases. After usual work up, a compound having m.p. 130-131°C was obtained.

Characterization of the compound, m.p. 130-131°C as 3β-iodo-6,6-ethylenedithio-5α-cholestane (CVIII)

The compound, m.p. 130-131°C was analyzed for C_{29}H_{49}S_{2}I (positive Beilstein test). The characteristic absorption bands in its IR spectrum were exhibited at 1435, 1245 (H₂C-S), and 510 cm⁻¹ (C-I). The NMR spectrum displayed a broad multiplet centred at δ 4.16 (W₂ = 14Hz; axial) ascribable to C3-α proton and a singlet at 3.15 which was attributed to four protons of dithiolane ring (-SCH₂CH₂S-). Methyl protons
were seen at $\delta$ 1.0 (ClO-CH$_2$), 0.68 (Cl$_3$-CH$_2$), 0.91 and 0.81 (other methyl protons). Thus from these observations the compound having m.p. 130-131° was regarded as 3β-iodo-6,6-ethylenedithio-5α-cholestane (CVIII).

**Reaction of 3α,5-cyclo-5α-cholestan-6-one (CIX) with 1,2-ethanedithiol**

The ketone (CIX) was similarly treated with 1,2-ethanedithiol in acetic acid using BF$_3$-etherate as catalyst. After usual work up of the reaction mixture and column chromatography over silica gel column, four compounds (CX-CXIII) were obtained.
Characterization of compound (CX) as 3α,5-cyclo-6,6-ethylene-dithio-5α-cholestan

Elemental analysis of the semi-solid (CX) corresponded to molecular formula C_{29}H_{48}S_{2}. The IR spectrum showed a band at 3030 cm\(^{-1}\) which indicated the presence of a three membered cyclic system (\(-\ce{C=C-}\)). Other IR bands were observed at 1435, 1255 (\(\ce{H=CH-S}\)) and 680 cm\(^{-1}\) (\(\ce{C-S}\)). The absence of a band for the carbonyl function suggested the incorporation of dithiolane ring in the molecule. Its NMR spectrum displayed a singlet integrating for four protons (\(-\ce{SCH_{2}CH_{2}S-}\)) at \(\delta\) 3.13 and a complex signal for cyclopropane ring protons at 0.6-0.4.
Methyl signals were observed at $\delta$ 1.0 (C10-CH$_3$), 0.72(C13-CH$_3$), 0.92 and 0.82 (for other methyl protons). Thus on the basis of these data the structure of the compound (CX) was established as 3$\alpha$,5-cyclo-6,6-ethylenedithio-5$\alpha$-cholestane.

Characterization of compound (CXI) as 3$\beta$-(2'-mercaptoethylthio)-5$\alpha$-cholestan-6-one

The compound (CXI), as an oil was analyzed for C$_{29}$H$_{50}$O$S_2$. Its IR spectrum exhibited a characteristic absorption band at 1735 cm$^{-1}$ which showed that carbonyl function remained unchanged during the reaction. Other important bands were observed at 2570 (-SH), 1425 and 1250 cm$^{-1}$ (H$_2$C-S). The NMR spectrum showed a multiplet centred at $\delta$ 2.9 for five protons (-SCH$_2$CH$_2$-, C3$\alpha$-H) where C3-proton was merged with four protons of the dithiolane ring. Another signal for one proton (-SH) was observed at $\delta$ 1.4. Methyl protons appeared at $\delta$ 1.2(C10-CH$_3$), 0.66 (C13-CH$_3$), 0.90 and 0.80 (for remaining methyl protons). On the basis of elemental analysis and spectral evidences, the compound CXI was characterized as 3$\beta$-(2'-mercaptoethylthio)-5$\alpha$-cholestan-6-one. This structure was further supported by the desulfurization of CXI with Raney nickel which furnished 5$\alpha$-cholestan-6-one (XCVI), m.p. 96$^\circ$ (reported m.p. 96$^\circ$).
Characterization of compound (CXII) as 5-(2'-mercaptoethylthio)-5α-cholestan-6-one

The compound (CXII) was analyzed for $C_{29}H_{50}O_{10}S_2$. The IR spectrum exhibited absorption bands at 2560 (–SH), 1710 (C=O), 1425 and 1265 cm$^{-1}$ ($H_2C-S-$). The NMR spectrum showed a singlet at $\delta$ 3.14 for four protons ($-S-CH_2-CH_2-S-$) and a broad signal at 1.35 for one proton ($-SH$). Methyl protons were observed at $\delta$ 1.1 ($C_{10}-CH_3$), 0.68 ($C_{13}-CH_3$), 0.91 and 0.81 (other methyl protons). Thus from the above elemental and spectral analyses data the structure of compound CXII was suggested to be 5-(2'-mercaptoethylthio)-5α-cholestan-6-one. This structure was further supported by its desulfurization with Raney nickel which yielded 5α-cholestan-6-one (XCVI), m.p. 96° (reported m.p. 96°).

Characterization of compound (CXIII) as 3β-(2'-mercaptoethylthio)-6,6-ethylenedithio-5α-cholestane

The semi-solid (CXIII) was analyzed for $C_{31}H_{54}S_4$. Its IR spectrum exhibited characteristic bands at 2565 (–SH), 1420, 1240 ($H_2C-S-$) and 705 cm$^{-1}$ (C=S). The absence of a band for the carbonyl function suggested the incorporation of dithiolane ring. The NMR spectrum showed a multiplet centred at $\delta$ 2.85 for nine protons ($2 \times -S-CH_2-CH_2-S-$ and $C3\alpha-H$) and a signal at 1.4 for one proton ($-SH$). Methyl
protons were seen at δ 1.0 (Cl0-CH3), 0.68 (Cl3-CH3), 0.90 and 0.80 (other methyl protons). These spectral data suggested the structure of compound CXIII as 3β-(2'-mercaptoethylthio)-6,6-ethylenedithio-5α-cholestane.

**Reaction of cholest-5-en-7-one (CXIV) with 1,2-ethanediethiol**

Cholest-5-en-7-one (CXIV) was treated with 1,2-ethanedithiol in acetic acid in the presence of BF$_3$-etherate as catalyst. After usual work up of the reaction mixture and removal of the solvent, a single semi-solid compound (CXV) was obtained in excellent yield.
Characterization of compound (CXV) as 7,7-ethylenedithiocholest-5-ene

The semi-solid compound (CXV) was analyzed for C_{29}H_{48}S_{2}. The absence of the band for carbonyl function in the IR spectrum suggested the incorporation of dithiolane ring in the molecule. The characteristic absorption bands were seen at 1645 (C=C), 1435 and 1225 cm\(^{-1}\) (H\(_2\)C=S). Its NMR spectrum displayed a singlet at \(\delta 5.36\) integrating for one proton which was ascribable to C-6 vinylic proton. Another singlet was observed at 3.23 for four protons of dithiolane ring (-S-CH\(_2\)-CH\(_2\)-S-). Methyl protons appeared at \(\delta 0.96\) (Cl\(_{10}\)-CH\(_3\)), 0.69 (Cl\(_{13}\)-CH\(_3\)), 0.90 and 0.80 (remaining methyl protons). On the basis of these data the structure of semi-solid compound (CXV) was established as 7,7-ethylenedithiocholest-5-ene. The structure of compound CXV was further supported by its desulfurization with Raney nickel which yielded cholest-5-ene (CXVI), m.p. 90\(^0\) (reported\(^{85}\) m.p. 89.5\(^0\)).

Reaction of 3\(^\beta\)-acetoxycholest-5-en-7-one (III) with 1,2-ethanedithiol

3\(^\beta\)-Acetoxycholest-5-en-7-one (III) on similar treatment with 1,2-ethanedithiol provided a compound having m.p.182-184\(^0\) in high yield (80\%).
Characterization of compound, m.p. 182-184° as 3β-acetoxy-7,7-ethylenedithiocholest-5-ene (IV)

Elemental analysis of compound (IV), m.p. 182-184° corresponded to molecular formula C_{31}H_{50}O_{5}S_{2} ([α]_{D}^{25} = -101.26°).
The IR spectrum exhibited characteristic bands at 1735 (\(-\text{COOCH}_3\)), 1645 (C=C), 1425 and 1235 cm\(^{-1}\) (H\(_2\)C=S). Its NMR spectrum displayed a singlet at \(\delta 5.63\) for C-6 vinylic proton, a broad multiplet for one proton at \(4.45\) (C3\(\alpha\)-H, \(J = 14\) Hz, axial)\(^{82}\) and another singlet integrating for four protons at 3.38 which was ascribable to the dithiolane ring protons (-S-CH\(_2\)CH\(_2\)S-).

A sharp singlet at \(\delta 2.02\) for three protons was assigned to acetoxy group protons (-OCOCH\(_3\)). Methyl protons were seen at \(\delta 1.06\) (Cl0-CH\(_3\)), 0.73 (Cl3-CH\(_3\)), 0.97 and 0.87 (other methyl protons). These data suggested the structure of the compound having m.p. 182-184\(^0\) as 3\(\beta\)-acetoxy-7,7-ethylene-dithiocholest-5-ene (IV). This structure was further confirmed by the desulfurization of IV with Raney nickel which yielded 3\(\beta\)-acetoxycholest-5-ene (C XVII), m.p. 114\(^0\) (reported\(^{85}\) m.p. 116\(^0\)).

**Reaction of 3\(\beta\)-chlorocholest-5-en-7-one (LXX) with 1,2-ethanedithiol**

The ketone (LXX) was treated with 1,2-ethanedithiol in the manner which was employed earlier. After usual work up and removal of the solvent, a compound melting at 125-126\(^0\) was obtained in good yield.
Characterization of compound, m.p. 125-126° as 3β-chloro-7,7-ethylenedithiocholest-5-ene (CXVIII)

The compound (CXVIII), m.p. 125-126° was analyzed for C_{29}H_{47}S_{2}Cl ([α]_{D}^{25} +120°). It gave positive Beilstein test for chlorine. The IR spectrum exhibited characteristic bands at 1645 (C=С), 1430, 1235 (H₂С-S) and 765 cm⁻¹ (C-Cl). Its NMR spectrum displayed a singlet at δ 5.65 for C-6 vinylic proton, a broad multiplet at 4.47 for C3-α proton (W₂ = 14Hz, axial) and another broad singlet at 3.42, integrated for four protons ascribable to dithiolane ring protons(-S-CH₂CH₂S). Methyl protons appeared at δ 1.08 (Cl0-CH₃), 0.71 (Cl3-CH₃), 0.94 and 0.84 (other methyl protons). On the basis of foregoing discussion, the compound having m.p. 125-126° was regarded as 3β-chloro-7,7-ethylenedithiocholest-5-ene (CXVIII). This
structure was further supported by the desulfurization of CXVIII with Raney nickel which furnished 3β-chlorocholesterol-5-ene (CXIX), m.p. 94-95° (reported87 m.p. 96°), \([\alpha]_D^{25.2} = -26°.

Oxidation of dithiolane (CXVIII) with m-chloroperbenzoic acid

3β-Chloro-7,7-ethylenedithiocholesterol-5-ene (CXVIII) was treated with m-chloroperbenzoic acid in CH₂Cl₂ at 10°. After the completion of reaction, it was taken in dichloromethane and washed with sodium bisulfite solution(10%). After work up and removal of the solvent, a single compound melting at 235°(decomposed) was obtained.
Characterization of the compound, m.p. 235° as 3β-chloro-7,7-ethylenedisulfonylcholest-5-ene (CXX)

The compound having m.p. 235° (decomposed) was analyzed for C_{29}H_{47}O_4S\textsubscript{2}Cl (positive Beilstein test). Its IR spectrum showed the characteristic bands at 1335 and 1130 cm\textsuperscript{-1} for the asymmetric and symmetric stretching of -SO\textsubscript{2} group. The other absorption bands were observed at 1620 (C=C), 740 (C-Cl) and 670 cm\textsuperscript{-1} (C-S). The NMR spectrum displayed a singlet at δ 5.5 for C-6 vinylic proton, a broad multiplet centred at 3.9 for C3α-\textsubscript{H} (J\textsubscript{ax} = 12Hz; axial), a broad signal for methylene (2 x -CH\textsubscript{2}) protons of dithiosulfonyl ring appeared at 3.65. The methyl signals were seen at δ 1.11 (C10-CH\textsubscript{3}), 0.71 (C13-CH\textsubscript{3}), 0.91 and 0.81 (other methyl protons). These spectral and elemental data suggested the structure for the compound (CXX) melting at 235° as 3β-chloro-7,7-ethylenedisulfonylcholest-5-ene.

Reaction of cholest-4-en-3-one (I) with 1,2-ethanedithiol

Cholest-4-en-3-one (I) was treated with 1,2-ethanedithiol in the same manner as applied earlier. After usual work up and removal of the solvent, a single compound, m.p. 108-110° was obtained in excellent yield (75%).
Characterization of the compound, m.p. 108–110° as 3,3-ethylenedithiocholest-4-ene (II)

Elemental analysis of the compound, m.p. 108–110° corresponded to formula C_{29}H_{48}S_{2}, [α]_{D}^{25} +127°. Important absorption bands at 1645 (C=C), 1425 and 1240 cm⁻¹ (H₂C=S) were seen in its IR spectrum. The NMR spectrum displayed a singlet at δ 5.52 for C-4 vinylic proton and another broad singlet at δ 3.2 which was assigned to four protons (-S-CH₂CH₂-S-) of dithiolane ring. Other signals were observed at δ 1.02 (Cl₀-CH₃), 0.68 (Cl₃-CH₃), 0.93 and 0.83 (for remaining methyl protons). From these observations the compound having m.p. 108–110° was characterized as 3,3-ethylenedithiocholest-4-ene (II). This structure was further supported
by its desulfurization with Raney nickel which yielded cholest-4-ene (CXXI), m.p. 77° (reported m.p. 79°), \([\alpha]^D_{25} +76°\).

Oxidation of dithiolane (II) with m-chloroperbenzoic acid

The dithiolane (II) was treated with m-chloroperbenzoic acid in CH₂Cl₂ at 10°. During work up, the reaction mixture was washed several times with sodium bisulfite solution (10%). Finally a compound, m.p. 215° (decomposed) was obtained.
Characterization of compound, m.p. 215° as 3,3-ethylenedisulfonylcholesterol-4-ene (CXXII)

Elemental analysis of the compound (CXXII), m.p. 215° (decomposed) corresponded to formula C_{29}H_{48}O_{4}S_{2}. The IR spectrum exhibited band at 1640 cm^{-1} (C=C) which showed that olefinic bond remained unaffected. The characteristic absorption bands appeared at 1340 and 1130 cm^{-1} for asymmetric and symmetric stretching of sulfone moiety. The NMR spectrum displayed a singlet at δ 5.35, assigned to C-4 vinylic proton and another singlet at δ 3.68 ascribable to four protons (4H, -S-CH_{2}CH_{2}-S-). Methyl protons were seen at δ 1.13 (Cl0-CH_{3}), 0.76 (Cl3-CH_{3}), 0.96 and 0.86 (for remaining methyl protons). On the basis of these data the compound melting at 215° (decomposed) was characterized as 3,3-ethylenedisulfonylcholesterol-4-ene (CXXII).
Thioethers

The general method by which thioethers can be easily prepared by the direct addition of sulfur or sulfur compounds to the unsaturated regions of organic compounds. Thioethers are known to act as convenient intermediates for the synthesis of different sulfur derivatives. Moreover, thioethers showed marked biological activities such as antiinflammatory, neurotropic, bactericidal, fungicidal and other similar properties. In this connection some work has already been done in our laboratory and in order to extend this work 3β-acetoxycholest-5-en-7-one (III) and its 3β-chloro analogue (LXX) have been subjected to the action of 2-mercaptoethanol and 3-mercaptopropan-1,2-diol in the presence of acetic acid and BF$_3$-etherate at room temperature.

In the earlier study$^{39a}$ from our laboratory the same ketones (III and LXX) were subjected to react with 2-mercaptoethanol in the presence of benzene and piperidine at the elevated temperature. In each case two isomeric thioethers (IIIa and IIIb) were isolated along with cholesta-3,5-dien-7-one (LXXI) as the minor product.
Reaction of 3β-acetoxycholest-5-en-7-one (III) with 2-mercaptoethanol

The ketone (III) in acetic acid was treated with 2-mercaptoethanol using $\text{BF}_3$-etherate as catalyst at room temperature for 30 min according to procedure of Fieser$^2$. Usual work up and fractionation by silica gel column chromatography yielded four compounds (CXXIII-CXXVI).
Characterization of compound, m.p. 88° as 3β-(2′-acetoxythioethoxy)cholest-5-en-7-one (CXXIII)

The compound (CXXIII), m.p. 88° was analyzed for \( \text{C}_{31}\text{H}_{50}\text{O}_{3}\text{S} \) (positive sodium nitroprusside test). Its IR spectrum exhibited bands at 1735 (\( \text{OCOCH}_3 \)), 1665 (\( \text{C=C-C=O} \)), 1425, 1245 (\(-\text{S-CH}_2\)) and 1030 cm\(^{-1}\) (\( \text{C-O} \)). The IR spectrum clearly indicated the presence of \( \alpha,\beta \)-unsaturated carbonyl function which remained unaltered during the reaction. The NMR spectrum displayed a singlet at \( \delta \) 5.68, ascribable to (\( \text{C}_6\text{-H} \)) vinylic proton, a triplet integrating for two protons 4.28 (\(-\text{SCH}_2\text{CH}_2\text{OAc} \)), a broad multiplet for three protons at 2.82 (\( \text{C}_3\alpha\text{-H} \) and \(-\text{SCH}_2\text{CH}_2\text{OAc} \)) and a three-proton singlet at 2.05 (\( \text{OCOCH}_3 \)). The methyl protons appeared at \( \delta \) 1.16 (\( \text{C}_{10}\text{-CH}_3 \)), 0.69 (\( \text{C}_{13}\text{-CH}_3 \)), 0.92 and 0.82 (remaining methyl protons). Thus from these observations the compound, m.p. 88° was regarded as 3β-(2′-acetoxythioethoxy)cholest-5-en-7-one (CXXIII).
An additional support for the formation of compound CXXIII was obtained by the study of its mass spectrum. The mass spectrum of compound (CXXIII) Scheme - 1 exhibited molecular ion peak at m/z 502 (with M+1 and M+2 peaks) and other important peaks at 487 (M -CH₃), 444, 443, 442 (M -CH₂-COOH, base peak), 415 (M -CH₂CH₂OAc), 414, 384, 382, (M -HSCH₂CH₂OAc), 367, 329 (442-side chain), 275, 269(382-side chain), 229, 187, 174 (382-C₁₅H₂₈), 161, 159, 135, 134, 107, 105, 95, 93, 91 and other low mass peaks. Mechanism for the formation of fragment ions at m/z 487, 442 and 382 is suggested in scheme-1. The mechanism is speculative in nature in the absence of isotopic labelling experiment or metastable peak evidence, however, confirms the proposed structure(CXXIII).

Scheme - 1

\[
m/z\ 487\ (M-\text{CH}_3)
\]
m/z 442 (M-CH$_3$COOH)

m/z 442 (C$_{29}$H$_{46}$O$_5$; base peak)

m/z 382 (M-HSCH$_2$CH$_2$OAc)

m/z 382 (C$_{27}$H$_{42}$O)

m/z 269 (382-side chain)

m/z 269 (C$_{19}$H$_{25}$O)
Characterization of the compound, m.p. 82° as 3α-(2'-acetoxythioethoxy)cholest-5-en-7-one (CXXIV)

The compound (CXXIV) m.p. 82° was analyzed for C₃₁H₅₀O₃S (positive sodium nitroprusside test). The IR spectrum showed bands at 1735 (OCOCH₃), 1665 (C=C–C=O), 1430, 1240 (–S–CH₂) and 1025 cm⁻¹ (C–O). It clearly showed that α,β-unsaturated carbonyl function remained unchanged and hydroxyl group was acetylated during the reaction. The NMR spectrum exhibited, a singlet at δ 5.6 ascribable to C-6 vinylic proton, two triplets each integrating for two protons at 4.3 (–SCH₂CH₂OAc) and 2.84 (–SCH₂CH₂OAc) and a multiplet for one proton at 3.32 (J₁ = 6Hz) which showed that C3-proton was equatorial. A sharp singlet of three protons appeared at δ 2.06 for acetoxy group protons. Methyl protons were seen at δ 1.18 (ClOT-CH₃), 0.68 (Cl₃-CH₃), 0.91 and 0.81 (remaining methyl protons). On the basis of above observations the compound, m.p. 82° was characterized as 3α-(2'-acetoxythioethoxy)cholest-5-en-7-one (CXXIV). The structure of CXXIV was further confirmed by the study of its mass spectrum.

The mass spectrum of (CXXIV) showed the molecular ion peak at m/z 502 alongwith (M+1) and (M+2) peaks. The other significant peaks were observed at 487 (M-CH₃), 459 (M-OCH₃), 443, 442 (M-CH₃COOH; base peak), 415 (M-CH₂CH₂OAc), 414, 383, 382 (M-HSCH₂CH₂OAc), 367 (382-CH₃), 329, 269 (382-side chain),
234, 187, 174 (382-C\textsubscript{15}H\textsubscript{20}), 161, 159, 135, 134, 107, 105, 95, 93, 91 and other low mass ion peaks. The mechanism for the formation of fragment ions m/z 487, 442 and 382 is similar to one given in case of (CXXIII).

The mass spectrometry in addition to and in conjunction with other instrumental techniques and chemical transformations offers a reliable method for differentiating the isomeric compounds (CXXIII and CXXIV). Table-1 records the relative intensity of molecular ion and the resultant ketonic ion for these isomeric compounds. From the ratio (between molecular ion and ketonic ion), one can plausibly conclude that the ejection of HSCH\textsubscript{2}CH\textsubscript{2}OAc is much more pronounced in that case (CXXIV) where sulfur is axially oriented.

Table - 1

| Ratio between intensity of molecular ion and ketonic ion. | CH\textsubscript{3}-OAc | C\textsubscript{8}H\textsubscript{17} | 1:8.51 |
Characterization of compound (CXXV) as 4α-(2'-acetoxymethoxy)cholest-5-en-7-one

Elemental analysis of the compound (CXXV) corresponded to formula \( C_{31}H_{50}O_3S \) (positive sodium nitroprusside test). Its IR spectrum exhibited characteristic bands at 1740, 1030 (OCOCH₃), 1665 (C=C-C=0), 1430 and 1235 cm⁻¹ (H₂C-S). In the NMR spectrum of CXXV, one-proton triplet appeared at \( \delta 3.65 \) (\( J = 12\text{Hz} \); axial) for C4β-proton which indicated that \(-\text{SCH}_2\text{CH}_2\text{OAc} \) group was equatorially (α) attached at C-4. Its NMR spectrum showed other signals at \( \delta 5.61\text{s} \) (1H, C6-H), 4.28t (2H, -CH₂OAc), 2.8t (2H, -SCH₂), 2.04s (3H, OCOCH₃), 1.0(C10-CH₃), 0.69 (C13-CH₃), 0.92 and 0.82 (remaining methyl protons). Thus on the basis of these data the product (CXXV) was characterized as 4α-(2'-acetoxymethoxy)cholest-5-en-7-one.
Characterization of compound (CXXVI) as 4α-(2'-hydroxythioethoxy)cholest-5-en-7-one

The semi-solid (CXXVI) was analyzed for C_{29}H_{48}O_{2}S (positive sodium nitroprusside test). Its IR spectrum showed characteristic bands at 3390 (-OH), 1665 (C=O-C=O), 1430 and 1240 cm^{-1} (H₂C-S). The NMR spectrum of (CXXVI) showed a triplet integrating for one proton at δ 3.68 (J = 12Hz, axial) for C₄β-proton suggesting -SCH₂CH₂OH group to be attached equatorially (α) at C-4. Other peaks in the NMR spectrum of compound CXXVI were seen at δ 5.62s (1H, C₆-H), 4.1t (2H, HOC₂H₂-), 2.88t (2H, -SCH₂), 1.16 (C₁₀-CH₃), 0.67 (C₁₃-CH₃), 0.91 and 0.81 (other methyl protons). On the basis of these data the structure of compound (CXXVI) was suggested to be 4α-(2'-hydroxythioethoxy)cholest-5-en-7-one. Acetylation of compound CXXVI with acetic anhydride and pyridine provided CXXV.

Reaction of 3β-chlorocholest-5-en-7-one (LXX) with 2-mercaptoethanol

When 3β-chlorocholest-5-en-7-one (LXX) was treated with 2-mercaptoethanol in the presence of BF₃-etherate as catalyst, it provided four compounds (CXXIII-CXXVI). These compounds were found identical (m.p., TLC, IR and NMR) with the compounds which were obtained earlier in the case of ketone III.
Reaction of 3β-chlorocholest-5-en-7-one (LXX) with 3-mercaptopropan-1,2-diol

The ketone (LXX) was allowed to react with 3-mercaptopropan-1,2-diol in the presence of acetic acid and BF₃-etherate according to the procedure of Fieser². After usual work up and fractionation by silica gel column chromatography seven compounds (CXVII-CXXIII) were obtained.
Acetylated compounds

(CXXXIV)

(CXXXV)
Characterization of compound (CXXXVII) as 3\(\beta\)-(3'-thiohydro-2'-acetoxypropoxy)-7-(5"-acetoxy-1"\(\alpha\),3\(\gamma\)\(\beta\)-oxathiane)cholest-5-ene

Elemental analysis of the compound (CXXXVII), a semi-solid corresponded to formula \(\text{C}_{37}\text{H}_{60}\text{O}_{6}\text{S}_{2}\) (negative Beilstein test and positive sodium nitroprusside test). Its IR spectrum did not show any band for the carbonyl function which suggested that the reagent has condensed with carbonyl function. This was evident from the characteristic absorption bands at 1420 (\(\text{H}_2\text{C}-\text{S} \text{ diff.})\), 1235 (\(\text{H}_2\text{C}-\text{S} \text{ wag.})\) and 1045 cm\(^{-1}\) (hemitioioketel ring vibration). The IR spectrum also gave a weak band at 2560 (\(-\text{SH}\)) and a strong band at 1740 cm\(^{-1}\) (\(\text{OCOCH}_2\)). Elemental analysis and IR spectrum suggested that chlorine at C-3 was substituted by -\(\text{OCH}_2\text{CHCH}_2\text{SH}\) group during the course of reaction.

Its NMR spectrum was more informative which showed a singlet at \(\delta 5.62\) for C-6 vinylic proton, two multiplets at 5.1 (2 \(\times\) \(\text{AcO-CH}^\ddagger\)) and 4.25 (C3\(\alpha\)-H, -\(\text{OCH}_2\)), for two and
four protons respectively, a distorted doublet for one proton
at 4.0 (\(-\text{OCH}_2\)), and other multiplet for four protons at
2.8 (2 \(\times\) \(-\text{SCH}_2\)). A sharp singlet for six protons appeared
at \(\delta\) 2.03 (2 \(\times\) \(-\text{OCOCH}_3\)). Methyl signals were seen at \(\delta\) 1.2
(\(-\text{ClO-CH}_3\)), 0.68 (\(-\text{Cl3-CH}_3\)), 0.93 and 0.83 (for other methyl
protons).

The configuration of hemithioketal ring was established
on the basis of the splitting pattern of \(-\text{OCH}_2\) and \(-\text{SCH}_2\)
protons (of hemithioketal ring). The appearance of a
distorted triplet for one proton of \(-\text{OCH}_2\) (of hemithioketal
ring) at \(\delta\) 4.0 and the merging of its \(-\text{OCH}_2\) other proton at
\(\delta\) 4.25 with other three \((\text{C}3\alpha-\text{H} \) and \(-\text{OCH}_2\)) protons at 4.25
clearly indicated that C7-O bond was axial or oxygen of
hemithioketal ring was axially (\(\alpha\)) oriented. It can be
explained by assuming that the methylene protons bonded with
the axially oriented oxygen atom were magnetically non-equi-
valent. Thus they behaved differently towards the applied
field and appeared at different chemical shifts in the spectrum
while methylene protons attached to the sulfur atom were almost
magnetically equivalent\(^{39b}\). The distortion in triplet might be
considered due to the long range coupling\(^{39b}\).

Thus on the basis of above data the compound (CXXVII)
was suggested to be \(3\beta-(3'-\text{thiohydro-2'-acetoxypropoxy})-7-\)
(\(5''\text{-acetoxy-1''}\alpha,3''\beta-\text{oxathiane})\text{cholest-5-ene}.

Characterization of the compound, m.p. 122-123° as 3β-(3'-thiohydro-2'-acetoxypropoxy)cholest-5-en-7-one (CXXVIII)

The compound, m.p. 122-123° was analyzed for C_{32}H_{52}O_{4}S (negative Beilstein Test). The IR spectrum exhibited characteristic bands at 2565 (weak, -SH), 1735 (OCOCH_{3}), 1665 (C=C-C=O), 1420, 1235 (H_{2}C-S) and 1030 cm^{-1} (C-O), it suggested that carbonyl function remained unaffected during the course of reaction. Its NMR spectrum gave a singlet at δ 5.58 for C-6 vinylic proton, two multiplets at 5.1 (1H,AcO-CH) and 4.2 (3H,-OCH_{2}, C3α-H), a two-proton doublet at 2.65 (-SCH_{2}) and sharp singlet for three protons at 2.04 (-OCOCH_{3}). Methyl protons appeared at δ 1.18 (Cl0-CH_{3}), 0.67 (Cl3-CH_{3}), 0.91 and 0.81 (for other methyl protons). These spectral data suggested the structure of compound having m.p. 122-123° as 3β-(3'-thiohydro-2'-acetoxypropoxy)cholest-5-en-7-one (CXXVIII).

Characterization of compound (CXXIX) as 3β-(3'-hydroxy-2'-acetoxythiopropoxy)cholest-5-en-7-one

Elemental analysis of compound (CXXIX), an oil corresponded to formula C_{32}H_{52}O_{4}S (negative Beilstein test). The IR spectrum displayed characteristic bands at 3360 (-OH), 1730 (-OCOCH_{3}), 1665 (C=C-C=O), 1425, 1235 (H_{2}C-S) and 1030 cm^{-1} (C-O). Its NMR spectrum showed a singlet at δ 5.61 for C-6 vinylic proton, two multiplets integrating for one and three protons respectively at 5.1 (AcO-CH) and 2.9 (-SCH_{2}, and C3α-H), a two-proton
doublet at 4.22 (-OCH₂) and a sharp singlet for three protons at 2.05 (-OCOCH₃). Methyl protons appeared at δ 1.18 (Cl0-CH₃), 0.67 (Cl3-CH₃), 0.91 and 0.81 (for remaining methyl protons). Thus on the basis of these spectral data the structure of compound CXXIX was established as 3β-(3'-hydroxy-2'-acetoxy-thiopropoxy)cholest-5-en-7-one.

Acetylation of CXXIX

The compound (CXXIX) on acetylation with acetic anhydride-pyridine provided 3β-(3',2'-diacetoxythiopropoxy)cholest-5-en-7-one (CXXXIV) as a semi-solid. This compound was analyzed for C₃₄H₅₄O₅S. The characteristic bands in its IR spectrum appeared at 1735 (-OCOCH₃), 1665 (C=C-C=O), 1425, 1230(H₂C-S) and 1030 cm⁻¹ (C-0). The NMR spectrum gave a singlet at δ 5.62 for C-6 vinylic proton. Two multiplets, each integrating for three protons at δ 5.2 (Ac0-CH, Ac0-CH₂) and 2.95 (-SCH₂, C3α-H), and a sharp singlet for six protons at 2.05(2 x OCOCH₃) were observed in the NMR spectrum. Methyl protons were seen at δ 1.2 (Cl0-CH₃), 0.69 (Cl3-CH₃), 0.93 and 0.83 (for other methyl protons).

Characterization of compound (CXXX) as 3β-(3'-thioacetyl-2'-hydroxypropoxy)cholest-5-en-7-one

The oily compound (CXXX) was analyzed for C₃₂H₅₂O₄S (negative Beilstein test). Its IR spectrum showed the
presence of α,β-unsaturated keto function (1660 cm⁻¹) which suggested that this function remained unaltered. The absorption bands at 3390 (-OH) and 1740 cm⁻¹ (-SCOCH₃) established that the -SH group was converted to mercaptoacetyl group during the course of reaction. Other IR bands were observed at 1420, 1235 (H₂C-S) and 1025 cm⁻¹ (C-O). The NMR spectrum of compound (CXXX) exhibited signals at δ 5.61s for C-6 vinylic proton, a multiplet for four protons at 3.95 (OCH₂, -OCH, C₃α-H), a two-proton doublet at 3.4 (AcS-CH₂) and a sharp singlet for three protons at 2.02 (-SCOCH₃).

Methyl protons appeared at δ 1.2 (C₁₀-CH₃), 0.67 (C₁₃-CH₃), 0.91 and 0.81 (other methyl protons). On the basis of these spectral data, the structure of compound (CXXX) was suggested to be 3β-(3'-thioacetyl-2'-hydroxypropoxy)cholest-5-en-7-one.

**Acetylation of CXXX**

Acetylation of compound (CXXX) with acetic anhydride-pyridine provided 3β-(3'-thioacetyl-2'-acetoxypropoxy)cholest-5-en-7-one (CXXXV) as an oil, which was analyzed for C₃₄H₅₄O₅S. The IR spectrum showed bands at 1735 (-SCOCH₃ and -OCOCH₃), 1665 (C=C-C=O), 1420, 1235 (H₂C-S-) and 1030 cm⁻¹ (C-O). The NMR spectrum displayed a one-proton singlet at δ 5.65 (C₆-H), two multiplets at 5.0 (AcO-CH) and 4.1 (-OCH₂, C₃α-H) for one and three protons respectively, a two-proton doublet at 3.35 (AcS-CH₂) and a broad singlet at 2.03 for six protons.
(-SCOCH₃, -OCOCH₃). The methyl protons appeared at δ 1.2 (Cl0-CH₃), 0.69 (Cl3-CH₃), 0.93 and 0.83 (for other methyl protons).

Characterization of compound (CXXXI) as 3β-(2'-hydroxy-2"-thioacetylisopropoxy)cholest-5-en-7-one

Elemental analysis of the compound (CXXXI) corresponded to molecular formula C₃₂H₅₂O₄S (negative Beilstein test). The IR spectrum exhibited characteristic bands at 3400 (–OH), 1740 (–SCOCH₃), 1660 (C=C–C=O), 1420 and 1240 cm⁻¹ (H₂C–S). Its NMR spectrum gave a singlet at δ 5.62 for C-6 vinylic proton, a four-proton multiplet centred at 4.27 (–OCH₂, OCH, C3a-H), a doublet integrating for two protons at 3.2 (AcS–CH₂) and a sharp singlet for three protons (–SCOCH₃) at 2.02. Methyl protons appeared at δ 1.2 (Cl0-CH₃), 0.69 (Cl3-CH₃), 0.92 and 0.82 (for remaining methyl protons). On the basis of these spectral data the oily compound (CXXXI) was characterized as 3β-(2'-hydroxy-2"-thioacetylisopropoxy)cholest-5-en-7-one.

Acetylation of CXXXI

On acetylation with acetic anhydride and pyridine, the compound CXXXI afforded 3β-(2'-acetoxy-2"-thioacetylisopropoxy)cholest-5-en-7-one (CXXXVI). This compound was analyzed for C₃₄H₅₄O₅S. Its IR spectrum gave a band at 1735 cm⁻¹ for –OCOCH₃ and –SCOCH₃. Other absorption bands appeared at
1660 (C=C-C=0), 1420, 1230 (H2C-S) and 1030 cm\(^{-1}\) (C=O). The NMR spectrum showed a singlet at \(\delta\) 5.65 for C-6 vinylic proton, two doublets, each integrating for two protons at 5.1 (AcO-CH\(_2\)) and 3.2 (AcS-CH\(_2\)), a two proton multiplet at 4.28 (-OCH, C3\(\alpha\)-H) and a singlet integrating for six protons at 2.03 (-OCOCH\(_3\), -SCOCH\(_3\)). Methyl protons appeared at \(\delta\) 1.18 (ClO-CH\(_3\)), 0.69 (Cl3-CH\(_3\)), 0.93 and 0.83 (for other methyl protons).

**Characterization of compound (CXXXII) as 4\(\alpha\)-(2'-hydroxy-2"-thioacetyl(isopropoxy)cholest-5-en-7-one**

Elemental analysis of the compound (CXXXII) corresponded to formula C\(_{32}\)H\(_{52}\)O\(_4\)S (negative Beilstein test). Its IR spectrum exhibited absorption bands at 3360 (-OH), 1735 (-SCOCH\(_3\)), 1660 (C=C-C=0), 1420 and 1230 cm\(^{-1}\) (H\(_2\)C-S) which suggested that \(\alpha,\beta\)-unsaturated keto function was unaffected and -SH group was converted to -SCOCH\(_3\) group during the course of reaction. The NMR spectrum showed a singlet at \(\delta\) 5.67s for C-6 vinylic proton, a multiplet for four protons at 4.32 (-OCH\(_2\), -OCH, C4\(\beta\)-H), a two-proton doublet at 3.5 (AcS-CH\(_2\)) and a sharp singlet for three protons at 2.01 (-SCOCH\(_3\)). Methyl protons were seen at \(\delta\) 1.16 (ClO-CH\(_3\)), 0.69 (Cl3-CH\(_3\)), 0.93 and 0.83 (for other methyl protons). Thus on the basis of these data the structure of compound (CXXXII) was established as 4\(\alpha\)-(2'-hydroxy-2"-thioacetyl(isopropoxy)cholest-5-en-7-one. 
Acetylation of CXXXII

Acetylation of compound (CXXXII) with acetic anhydride-pyridine provided 4α-(2'-acetoxy-2''-thioacetylisopropoxy)cholest-5-en-7-one (CXXXVII). Its elemental analysis corresponded to formula \( C_{34}H_{54}O_5S \). The IR spectrum displayed characteristic absorption bands at 1735 (-SCOCH₃, -OCOCH₃), 1660 (C=C-C=O), 1420 and 1235 cm⁻¹ (H₂C-S-). Its NMR spectrum showed signals at δ 5.68s (1H, C6-H), 5.1d (2H, AcO-CH₂), 4.28m (2H, -OCH, C4β-H), 3.45d(2H, AcS-CH₂) and 2.03s (6H, -OCOCH₃, -SCOCH₃). Methyl protons appeared at δ 1.2 (Cl0-CH₃), 0.69 (Cl3-CH₃), 0.94 and 0.84 (for other methyl protons).

Characterization of compound (CXXXIII) as 4α-(3'-acetoxy-2'-hydroxythiopropoxy)cholest-5-en-7-one

The compound (CXXXIII) was analyzed for \( C_{32}H_{52}O_4S \) (negative Beilstein test). The characteristic absorption bands in its IR spectrum appeared at 3360 (-OH), 1730 (-OCOCH₃), 1660 (C=C-C=O), 1415, 1230 (H₂C-S-) and 1030 cm⁻¹ (C-O). The NMR spectrum displayed a singlet at δ 5.65 for C-6 vinylic proton, a two-proton doublet at 5.1 (AcO-CH₂), two multiplets integrating for one and three protons respectively, were centred at 4.3 (-OCH) and 2.85 (-SCH₂, C4β-H) and a three-proton singlet at 2.05 (-OCOCH₃). The methyl protons were seen at δ 1.18 (Cl0-CH₃), 0.68 (Cl3-CH₃), 0.92 and 0.82 (for remaining methyl protons). These spectral data suggested
the structure of compound (CXXXIII) to be 4α-(3'-acetoxy-2'-hydroxythiopropoxy)cholest-5-en-7-one.

**Acetylation of CXXXIII**

The compound (CXXXIII) on acetylation with acetic anhydride-pyridine afforded 4α-(3',2'-diacetoxythiopropoxy) cholest-5-en-7-one (CXXXVIII) as a semi-solid, which was analyzed for C_{34}H_{54}O_{5}S. The IR spectrum exhibited bands at 1730 (–OCOCH₃), 1660 (C=O), 1420, 1235 (H₂C=S⁻) and 1030 cm⁻¹ (C–O). Its NMR spectrum showed a singlet at δ 5.68 for C-6 vinylic proton, two multiplets each integrating for three protons were centred at 5.15 (AcO-CH₂, AcO-CH), 2.8 (–SCH₂, C₄H₂) and a six-proton singlet at 2.05 (2 x –OCOCH₃). Methyl protons appeared at δ 1.18 (Cl₀-CH₃), 0.69 (Cl₃-CH₂), 0.93 and 0.83 (for other methyl protons).

**Reaction of 3β-acetoxycholest-5-en-7-one (III) with 3-mercapto-propan-1,2-diol**

The ketone (III) was treated with 3-mercapto-propan-1,2-diol in the presence of acetic acid and BF₃-etherate in the manner employed previously. After usual work up and fractionation by silica gel column chromatography, two compounds m.p. 122-123⁰ and 134-135⁰ were obtained. The compound m.p. 122-123⁰ was characterized as 3β-(3'-thiohydro-2'-acetoxypropoxy)cholest-5-en-7-one (CXXVIII) and was found identical.
(m.p., TLC, IR and NMR) with the compound (CXXVIII) obtained from the reaction of 3-mercaptopropan-1,2-diol with ketone (LXX) earlier.

\[
\begin{align*}
&\text{(III)} & \text{(CXXVIII)} & \text{(CXXXIX)} \\
&\text{AcO} & \text{AcO-CH} & \text{H}_2\text{C}-\text{O}^\delta \text{H} \\
&\text{CH}_2\text{SH} & \text{CH}_2\text{OH} & \text{CH}_2\text{OAc} \\
&\text{BF}_3\text{-etherate} & & \\
&\text{AcOH} & & \\
&\text{AcO-CH} & & \\
&\text{CH}_2\text{SH} & & \\
\text{H}_2\text{C-S} & & \\
&\text{H} & & \\
\text{H}_2\text{C-OH} & & \\
&\text{CH}_2\text{OAc} & & \\
\end{align*}
\]

Characterization of the compound, m.p. 134-135°C as 38-(3'-acetoxy-2'-hydroxythiopropyloxy)cholest-5-en-7-one (CXXXIX)

The compound having m.p. 134-135°C was analyzed for 
\(\text{C}_{32}\text{H}_{52}\text{O}_{4}\text{S}\). Its IR spectrum exhibited characteristic absorption bands at 3400 (-OH), 1735 (-OCOCH_3), 1665(C=C-C=0), 1420, 1235 (H_2C-S-) and 1030 cm\(^{-1}\) (C-O). The NMR spectrum gave a singlet at \(\delta 5.59\) for C-6 vinylic proton, a two-proton doublet at 5.0 (AcO-CH\(_2\)), two multiplets integrating for one
and three protons respectively were centered at 4.1 (-OCH) and 2.85 (-SCH₂, C3α-Η) and a sharp singlet for three protons at 2.04 (-OCOCH₃). Methyl protons appeared at δ 1.16 (C10-CH₃), 0.67 (C13-CH₃), 0.91 and 0.81 (for remaining methyl protons). Thus the above data established the structure of compound having m.p. 134-135°C as 3β-(3'-acetoxy-2'-hydroxy-thiopropoxy)cholest-5-en-7-one (CXXXIX).

Acetylation of CXXXIX

The compound (CXXXIX) on similar treatment with acetic anhydride-pyridine provided 3β-(3',2'-diacetoxythiopropoxy) cholest-5-en-7-one (CXXXIV) as a semi-solid. The same compound was also obtained earlier on acetylation of CXXIX with acetic anhydride and pyridine.
Experimental

All melting points were observed on a Kofler apparatus and are uncorrected. Infrared (IR) spectra were recorded in Nujol with a Perkin-Elmer 237 spectrophotometer. IR values are given in cm$^{-1}$. NMR spectra were run in CDCl$_3$ or CCl$_4$ on a Varian A60 instrument with Me$_4$Si(TMS) as internal standard and its values are given in ppm(δ). Mass spectra were measured on a AIE MS-9 mass spectrometer. The values in parentheses are the relative abundance (%) of the peaks with respect to base peak as 100%. Thin layer chromatographic (TLC) plates were coated with silica gel G and a 20% aqueous solution of perchloric acid was used as spraying agent. Light petroleum refers to a fraction of b.p. 60-80°. Anhydrous sodium sulfate (Na$_2$SO$_4$) was used as a drying agent. The abbreviations "s, d, t, br and mc!", denote "singlet, doublet, triplet, broad and multiplet centred at", respectively.

3β-Chlorocholest-5-ene

Freshly purified thionyl chloride (15 ml) was added to cholesterol (20 g) at room temperature. A vigorous reaction
ensued with the evolution of gaseous products. When the reaction slackened, the mixture was gently heated at a temperature of 50-60° on a water bath for 30 min and then poured onto crushed ice with stirring. The yellow solid thus obtained was filtered under suction and washed several times with ice-cooled water and air-dried. Recrystallization from acetone gave 3β-chlorocholest-5-ene (19.2 g), m.p. 95-96° (reported m.p. 96-97°). It gave positive Beilstein test and a yellow color with tetranitromethane in chloroform.

**Cholest-5-ene**

3β-Chlorocholest-5-ene (10.0 g) was dissolved in warm amyl alcohol (200 ml) and sodium metal (24 g) was added in small portions to the solution with continuous stirring over a period of 8 hr. The reaction mixture was heated occasionally during the course of reaction in order to keep the sodium metal dissolved. The reaction mixture was poured into water, acidified with HCl and allowed to stand overnight. A white crystalline solid thus obtained was filtered under suction and washed thoroughly with water and air-dried. Recrystallization of crude material from acetone gave cholest-5-ene in cubes (7.2 g), m.p. 92-93° (reported m.p. 89.5-91.2°).
6-Nitrocholest-5-ene

A suspension of finely powdered cholest-5-ene (3.0 g) in glacial acetic acid (25 ml) was stirred at room temperature for 5 min. Fuming nitric acid (10 ml; sp. gr. 1.52) was rapidly added. Sodium nitrite (1.5 g) was added gradually over a period of 1 hr with stirring and the stirring was continued for 2 hr. The temperature of the reaction mixture was controlled between 20-25° by external cooling. A yellow solid thus obtained was filtered under suction, washed thoroughly with water and air-dried. Recrystallization from methanol furnished 6-nitrocholest-5-ene (1.6 g), m.p. 117-118° (reported 117-118°).

5α-Cholestan-6-one (XCVI)

6-Nitrocholest-5-ene (3.0 g) was dissolved in glacial acetic acid (100 ml) by heating and to this solution zinc dust (6.0 g) was added in small portions. After the initial exothermic reaction had subsided, the suspension was heated under reflux for 3 hr and water (6 ml) was added now and then during the course of reaction. The solution was then filtered and the residue was washed with two 10 ml portions of warm acetic acid. To the filtrate was added a few ml of water till turbidity developed and it was allowed to stand overnight at room temperature. The crystalline material
thus separated was filtered under suction and washed thoroughly with water in order to remove zinc acetate. The organic solid was air-dried and its recrystallization from ethanol afforded 5α-cholestan-6-one (XCVI) (1.8 g), m.p. 94-95° (reported\textsuperscript{84} m.p. 95-96°).

3β-Acetoxycholest-5-ene

A mixture of cholesterol (20.0 g), freshly distilled pyridine (30 ml) and acetic anhydride (20 ml) was heated on a steam bath for 2 hr. The resulting brown solution was poured onto crushed ice-water mixture with stirring. A light brown solid was obtained which was filtered under suction, washed with water until free from pyridine and air-dried. The crude product on recrystallization from acetone gave the pure 3β-acetoxycholest-5-ene (18.0 g), m.p. 114-115° (reported\textsuperscript{86} m.p. 116°).

3β-Acetoxy-6-nitrocholest-5-ene

3β-Acetoxycholest-5-ene (5.0 g) was covered with nitric acid (125 ml; sp. gr. 1.52). Sodium nitrite (5.0 g) was gradually added over a period of 1 hr with continuous stirring. Slight cooling was also required during the course of the reaction and the stirring was continued for additional 2 hr. A yellow spongy mass was separated on the surface of
the mixture, it was diluted with cold water (100 ml), then a green colored solution was obtained. The whole mass was extracted with ether. The ethereal layer was washed with water, NaHCO₃ solution (5%) (until washing become pink) and water, and dried (Na₂SO₄). Removal of the solvent provided the nitro compound as an oil which was crystallized from methanol (with traces of acetone) (3.5 g), m.p. 104° (reported m.p. 102-104°).

3β-Acetoxy-5α-cholestan-6-one (III)

3β-Acetoxy-6-nitrocholest-5-ene (3.0 g) was dissolved in glacial acetic acid (125 ml) by warming the mixture and zinc dust (6.0 g) was added in small portions with shaking. The suspension was heated under reflux for 4 hr and water (6 ml) was added now and then during the course of reduction. The hot solution was filtered, cooled to room temperature and diluted with a large excess of ice-cooled water. The precipitate thus obtained was taken in ether and the ethereal solution was washed with NaHCO₃ solution (10%) and water, and then dried (Na₂SO₄). Evaporation of the solvent gave the acetoxy ketone (III) as an oil which was crystallized from methanol (2.1 g), m.p. 128-129° (reported m.p. 127-128°).

3β-Chloro-6-nitrocholest-5-ene

To a well stirred mixture of 3β-chlorocholest-5-ene
(6 g), glacial acetic acid (50 ml) and nitric acid (12.5 ml, sp. gr. 1.52) at room temperature, was added sodium nitrite (1.8 g) gradually. After the complete addition of sodium nitrite, the mixture was further stirred for 1 hr. The content was diluted by the addition of water (100 ml) and the stirring was continued for 10 min more. The yellowish solid thus separated was filtered and air-dried. The desired product was recrystallized from methanol as needles (3.6 g), m.p. 150-152° (reported m.p. 153°).

3β-Chloro-5α-cholestan-6-one (CII)

To a solution of 3β-chloro-6-nitrocholest-5-ene (3.0 g) in hot glacial acetic acid (70 ml), zinc dust (6 g) was added gradually in small portions with constant shaking. The suspension was heated under reflux for 4 hr and water (6 ml) was added at regular intervals during the course of heating. The hot solution was filtered to remove unreacted zinc and the filtrate was cooled to room temperature, followed by dilution with excess of ice-cooled water. The organic matter was extracted with ether and ethereal solution was washed with NaHCO₃ solution (10%) and water, and dried (Na₂SO₄). Evaporation of the solvent gave an oil which was crystallized from methanol (1.9 g), m.p. 127-129° (reported m.p. 129°).
3α,5-Cyclo-5α-cholestan-6-one (CIX)

A mixture of 3β-chloro-5α-cholestan-6-one (CII) (2.0 g) and methanolic potash (30 ml containing 1.6 g of KOH) was heated under reflux for 1 hr and the reaction mixture was poured into water. It was extracted with ether and the ethereal layer was washed several times with water, and dried (Na₂SO₄). After removal of the solvent the cycloketone (CIX) was obtained which was crystallized from methanol (1.2 g), m.p. 96-97° (reported m.p. 97°).

3β-Bromo-5α-cholestan-6-one (CV)

3α,5-Cyclo-5α-cholestan-6-one (CIX) (1.0 g) was heated under reflux with hydrobromic acid (1.25 ml; 48%) in acetone (3.7 ml) for about 6 hr. Most of the solvent was removed under reduced pressure and the residue was diluted with water (10 ml). A solid thus obtained was recrystallized from methanol to give the bromoketone (CV) (0.8 g), m.p. 120-121° (reported m.p. 123°).

3β-Iodo-5α-cholestan-6-one (CVII)

3α,5-Cyclo-5α-cholestan-6-one (CIX) (1.7 g) was dissolved in acetic acid (25 ml) and treated with HI (5 ml; 54%). The turbid solution was made clear by addition of ether. The mixture was kept at room temperature for 20 hr and then it
was poured into ice-cooled water and extracted with ether. The ethereal layer was washed with water, NaHCO₃ solution (5%) and finally with water, and dried (Na₂SO₄). Removal of the solvent gave an oil which was crystallized from methanol to give the iodoketone (CVII) (1.27 g), m.p. 136-137°C (reported m.p. 137-138°C).

Cholest-5-en-7-one (XCIV)

A solution of t-butyl chromate [t-butyl alcohol (60 ml), CrO₃ (20.0 g), acetic acid (84 ml), acetic anhydride (10 ml)] was added at 0°C to a solution of cholest-5-ene (8.0 g) in CCl₄ (150 ml), acetic acid (30 ml) and acetic anhydride (10 ml). The content was refluxed for 3 hr and then it was diluted with water. The organic layer was washed with NaHCO₃ solution (5%) and water, and dried (Na₂SO₄). Evaporation of the solvent under reduced pressure provided cholest-5-en-7-one (XCIV) as an oil which was crystallized from methanol (3.1 g), m.p. 128°C (reported m.p. 125-129°C).

3β-Acetoxycholest-5-en-7-one (III)

A solution of t-butyl chromate [t-butyl alcohol (60 ml), CrO₃ (20 g), acetic acid (85 ml) and acetic anhydride (10 ml)] was added at 0°C to a solution of 3β-acetoxycholest-5-ene (8 g) in carbon tetrachloride (150 ml), acetic acid (30 ml) and
acetic anhydride (10 ml). The content was refluxed for 3 hr and then it was washed with NaHCO₃ solution (5%), water, and dried (Na₂SO₄). Evaporation of the solvent under reduced pressure furnished the compound (III) as an oil which was crystallized from methanol (3.2 g), m.p. 161-163°C (reported 97 m.p. 164°C).

3β-Chlorocholest-5-en-7-one (LXX)

A solution of t-butyl chromate [t-butyl alcohol (60 ml), CrO₃ (20 g), acetic acid (35 ml) and acetic anhydride (10 ml)] 96 was added at 0°C to a solution of 3β-chlorocholest-5-ene (8 g) in carbon tetrachloride (150 ml), acetic acid (30 ml) and acetic anhydride (10 ml). The content was refluxed for 3 hr and then it was washed with NaHCO₃ solution (5%) and water, and dried (Na₂SO₄). Evaporation of the solvent under reduced pressure furnished the ketone (LXX) as an oil which was crystallized from methanol (3.30 g), m.p. 144°C (reported 98 m.p. 144-145°C).

3β-Hydroxy-5,6β-dibromo-5α-cholestane

To a solution of cholesterol (14 g) in ether (100 ml) was added gradually the bromine solution (9.6 g in 100 ml of acetic acid containing 1 g of anhydrous sodium acetate). The solid thus obtained was filtered under suction and washed with cold ether:acetic acid mixture (3:7). The dried dibromide
3β-Hydroxy-5,6β-dibromo-5α-cholestan-3-one (10 g) was suspended in acetone (300 ml). The suspension was cooled to 0-5°. It was stirred for 5 min and to this mixture, Jones' reagent was added dropwise over a period of 20 min at the maintained temperature of 0-5°. Water (200 ml) was added and dibromo-ketone was filtered under suction, washed with water, methanol and air-dried. (9 g), m.p. 73-75° (reported m.p. 73-75°).

Cholest-5-en-3-one

To a solution of 5,6β-dibromo-5α-cholestan-3-one (5 g) in ether (100 ml) was added glacial acetic acid (2.5 ml). Zinc dust (7.5 g) was added in small portions during 30 min with continuous shaking. After complete addition, the ethereal solution containing zinc dust was filtered, washed with water, NaHCO₃ solution (5%) and water, and dried (Na₂SO₄). Removal of the solvent provided an oil which was crystallized from methanol (3.3 g), m.p. 126-127° (reported m.p. 129°).

Cholest-4-en-3-one (I)

Cholest-5-en-3-one (4.0 g) was dissolved in ethanol (40 ml) and to this was added a solution of oxalic acid (0.5 g)
in ethanol (5 ml). The reaction mixture was refluxed for 15 min then allowed to stand at room temperature. Crystallization occurred after 1 hr and to ensure complete crystallization, it was cooled at 0-4° and then filtered. The crude product was recrystallized from methanol to give the ketone (I) (3.0 g), m.p. 80° (reported m.p. 81-82°).

Reaction of 5α-cholestan-6-one (XCVI) with 1,2-ethanedithiol using BF₃-etherate as a catalyst

The solution of 5α-cholestan-6-one (2.0 g) in acetic acid (60 ml) was treated with ethanedithiol (1.123 g; 11.94 mmol) and freshly distilled BF₃-etherate (2 ml), and kept at room temperature for 1 hr. The solution was diluted with methanol (10 ml), poured into water and extracted with ether. The ethereal layer was washed successively with water, sodium bicarbonate solution (5%), and water and dried over anhydrous sodium sulfate. After removal of the solvent, 6,6-ethylenedithio-5α-cholestane (XCVII) as a semi-solid (1.5 g) was obtained.

Analysis Found : C, 75.27; H, 10.79

C₂₉H₅₀S₂ requires : C, 75.32; H, 10.82%.

IR : νₘₐₓ. 1430, 1245 cm⁻¹ (H₂C-S-)

NMR : δ 3.0s (4H, -S-CH₂-CH₂-S-), 1.20 (Cl₅-CH₃), 0.67 (Cl₃-CH₃), 0.91 and 0.81 (other methyl protons).
Desulfurization of compound (XCVII) with Raney nickel

6,6-Ethylendithio-5α-cholestane (XCVII) (0.3 g) in absolute ethanol (200 ml) was refluxed with Raney nickel (3 g) for 20 hr. The suspension was filtered. After removal of the solvent 5α-cholestane (XCVIII) was obtained which was recrystallized from acetone (0.09 g), m.p. 80-81° (reported m.p. 80°).

Oxidation of dithiolane (XCVII) with m-chloroperbenzoic acid

The dithiolane (XCVII) (0.462 g) was dissolved in dichloromethane (90 ml) and cooled in ice bath to 10° and stirred. To this ice cooled stirring reaction mixture, m-chloroperbenzoic acid (0.2 g) was added in fractions during 30 min. Stirring was continued for another 2½ hr. Complete conversion of starting material was evidenced by TLC. Reaction mixture was worked up with CH₂Cl₂, washed with sodium bisulfite solution (10%) to destroy unreacted peracid and then with water, and dried (Na₂SO₄). Removal of the solvent and purification by silica gel column provided 6,6-ethylene-disulfanyl-5α-cholestane (XCIX) as a viscous liquid (0.31 g).

Analysis Found : C, 70.45; H, 10.09

C₂₉H₅₀O₂S₂ requires : C, 70.44; H, 10.12%

IR : C = O max. 1060 ( S=O), 670 cm⁻¹ (C-S)

NMR : δ 3.32 br, s (4H, -SO-CH₂-CH₂-SO-), 1.23 (Cl₃-CH₃), 0.73 (Cl₅-CH₃), 0.93 and 0.83 (other methyl protons).
Reaction of 3β-acetoxy-5α-cholestan-6-one (C) with 1,2-ethanedi-thiol using BF₃-etherate as a catalyst

3β-Acetoxy-5α-cholestan-6-one (C) (2.0 g) dissolved in acetic acid (60 ml) was treated with 1,2-ethanedi-thiol (1.123 g; 11.94 mmol) and added BF₃-etherate (2 ml). After completion of the reaction it was diluted with methanol (10 ml). Usual work up and removal of the solvent yielded 3β-acetoxy-6,6-ethylene-dithio-5α-cholestane (CI), recrystallized from acetonitrile (1.75 g), m.p. 149-151°C.

Analysis Found : C, 71.47; H, 9.97
C₃₁H₅₂O₂S₂ requires : C, 71.54; H, 10.0%
IR : ν max. 1747, 1035 (-OCOCH₃), 1435, 1245 (CH₂-S)
       675 cm⁻¹ (C-S).
NMR : δ 4.7mc (C₃-αH; W₁ = 14Hz; axial), 3.18s (-S-CH₂-CH₂S-)
       2.08s (-OCOCH₃), 1.18 (Cl0-CH₃), 0.68 (Cl3-CH₃), 0.90
       and 0.80 (other methyl protons).

Reaction of 3β-chloro-5α-cholestan-6-one (CII) with 1,2-ethanedi-thiol using BF₃-etherate as catalyst

3β-Chloro-5α-cholestan-6-one (CII) (1.0 g) was treated with 1,2-ethanedi-thiol (0.56 g; 5.95 mmol) in the presence of BF₃-etherate (1 ml) and the reaction mixture was allowed to stand at room temperature for 1 hr. The solution was
diluted with methanol (5 ml), poured into water and extracted with ether. The ethereal layer was washed successively with water, NaHCO₃ solution (5%) and water, and dried (Na₂SO₄). Removal of the solvent afforded 3β-chloro-6,6-ethylenedithio-5α-cholestane (CIII), recrystallized from acetonitrile (0.85 g), m.p. 143°.

Analysis Found : C, 70.05; H, 9.85
C₂₉H₄₉S₂Cl requires : C, 70.09; H, 9.87%
IR : ν max. 1430, 1240 (H₂C-S), 760 (C-Cl), 675 cm⁻¹ (C-S)
NMR : δ 3.9br, m (1H, C₃α-H; W₂ = 16Hz; axial), 3.1s (4H, -SCH₂CH₂S-), 1.06 (C₁₀-CH₃), 0.73 (C₁₃-CH₃), 0.96 and 0.80 (remaining methyl protons).

Desulfurization of CIII with Raney nickel

The dithiolane (CIII) (0.35 g) in absolute ethanol (225 ml) was refluxed with Raney nickel (3.5 g) for 20 hr and then the suspension was filtered. Removal of the solvent gave 3β-chloro-5α-cholestane (CV), recrystallized from acetone (0.1 g), m.p. 113° (reported m.p. 115°).

Reaction of 3β-bromo-5α-cholestan-6-one (CV) with 1,2-ethanedithiol and BF₃-etherate as catalyst

The bromoketone (CV), (1.0 g) was treated with 1,2-ethanedithiol (0.56 g; 5.95 mmol) in the presence of BF₃-etherate in the manner employed earlier. After usual work up
and recrystallization from acetonitrile, 3β-bromo-6,6-ethylene-
dithio-5α-cholestan (CVI) (0.8 g), m.p. 139-140° was obtained.

Analysis Found : C, 64.31; H, 9.01

C₂₉H₄₉S₂Br requires : C, 64.32; H, 9.05%

IR : $\nu_{\text{max.}}$ 1435, 1240 (H₂C-S), 680 (C-S), 670 cm⁻¹ (C-Br)

NMR : δ 3.9br, m (1H, C₃α-H; W₂ = 15Hz, axial), 3.11s (4H, -SCH₂CH₂S-), 0.93 (Cl₀-CH₃), 0.63 (Cl₃-CH₂), 0.86
and 0.78 (other methyl protons).

Reaction of 3β-iodo-5α-cholestan-6-one (CVII) with 1,2-ethane-
dithiol using BF₃-etherate as catalyst

The iodoketone (CVII (1.0 g) was treated with 1,2-ethane-
dithiol (0.56 g; 5.95 mmol) in the presence of BF₃-etherate in
the same manner. After usual work up and recrystallization
from acetonitrile, 3β-iodo-6,6-ethylenedithio-5α-cholestan
(CVIII), (0.85 g), m.p. 131° was obtained.

Analysis Found : C, 59.18; H, 8.29

C₂₉H₄₉S₂I requires : C, 59.19; H, 8.33%

IR : $\nu_{\text{max.}}$ 1435, 1245 (H₂C-S), 510 cm⁻¹ (C-I)

NMR : δ 4.16br, m (1H, C₃α-H, W₂ = 14Hz, axial), 3.15s
(4H,-SCH₂CH₂S-), 1.0 (Cl₀-CH₂), 0.68 (Cl₃-CH₃), 0.91
and 0.81 (other methyl protons).
Reaction of 3α,5-cyclo-5α-cholestan-6-one (CIX) with 1,2-ethanedithiol using BF$_3$-etherate as a catalyst

The ketone (CIX) (3.0 g) in acetic acid (90 ml) was treated with 1,2-ethanedithiol (1.68 g; 17.87 mmol) and freshly distilled BF$_3$-etherate (2 ml) at room temperature for 1 hr. It was diluted with methanol (10 ml). After usual work up and removal of the solvent, it gave an oil which was chromatographed over silica gel column. Elution with light petroleum:ether (15:1) gave 3α,5-cyclo-6,6-ethylenedithio-5α-cholestane (CX) as a non-crystallizable semi-solid (1.44 g).

Analysis Found: C, 75.62; H, 10.45

Analysis Required: C, 75.65; H, 10.43%

IR: $\nu_{\max}$ 3030 (C=C), 1435, 1255 (H$_2$C-S), 680 cm$^{-1}$ (C-S)

NMR: $\delta$ 3.13s (4H, -S-CH$_2$CH$_2$-S), 1.0 (ClO-CH$_3$), 0.72(C13-CH$_3$), 0.92, 0.82 (other methyl protons) and 0.6-0.4 (a complex signal of cyclopropane ring protons).

Further elution with light petroleum:ether (12:1) provided 3β-(2'-mercaptoethylthio)-5α-cholestan-6-one (CXI) as an oil (0.56 g).

Analysis Found: C, 78.83; H, 10.42

Analysis Required: C, 78.80; H, 10.46%

IR: $\nu_{\max}$ 2570 weak (-SH), 1735 (C=O), 1425, 1250 cm$^{-1}$ (H$_2$C-S-).
NMR : δ 2.9m (5H, -SCH₂CH₂S-, C3α-H), 1.4 (-SH), 1.2 (C10-CH₃), 0.66 (C13-CH₃), 0.90 and 0.80 (other methyl protons).

Continued elution with light petroleum:ether (11:1) gave 5-(2'-mercaptoethylthio)-5α-cholestan-6-one (CXII) as an oil (0.26 g).

Analysis Found : C, 72.78; H, 10.48
C₂₉H₅₀O₂S₂ requires : C, 72.80; H, 10.46%
IR : νmax. 2565 weak (-SH), 1710 (C=O), 1425, 1265 cm⁻¹ (H₂C-S-)
NMR : δ 3.14s (4H, -SCH₂CH₂S-), 1.35 (-SH), 1.1 (C10-CH₃), 0.68 (C13-CH₃), 0.91 and 0.81 (other methyl protons).

Further elution with light petroleum:ether (9:1) afforded 3β-(2'-mercaptoethylthio)-6,6-ethylendithio-5α-cholestane (CXIII) as a non-crystallizable semi-solid (1.3 g).

Analysis Found : C, 67.12; H, 9.70
C₃₁H₅₄S₄ requires : C, 67.15; H, 9.74%
IR : νmax. 2565 weak (-SH), 1420, 1240 (H₂C-S-), 705 cm⁻¹ (C-S).
NMR : δ 2.85m (9H, 2 x -SCH₂CH₂S-, C3α-H), 1.4 (-SH), 1.0 (C10-CH₃), 0.68 (C13-CH₃), 0.90 and 0.80 (other methyl protons).
Desulfurization of compounds (CXI) and (CXII)

Compound (CXI) (0.2 g) in absolute ethanol on refluxing with Raney nickel provided a compound (0.09 g) having m.p. 96° which was found identical with the authentic sample of 5α-cholestan-6-one (CXVI).  

Similar treatment of compound (CXII) (0.1 g) with Raney nickel also afforded 5α-cholestan-6-one (CXVI) (0.04 g), m.p. 96°.  

Reaction of cholest-5-en-7-one (XCIV) with 1,2-ethanedithiol using BF₃-etherate as a catalyst

Cholest-5-en-7-one (XCIV) (2.0 g) was dissolved in 60 ml of acetic acid and treated with 1,2-ethanedithiol (0.98 g; 10.42 mmol) in the presence of BF₃-etherate (2 ml) as a catalyst at room temperature. After 1 hr it was diluted with methanol (10 ml) and poured into water. After usual work up and removal of the solvent the reaction mixture afforded 7,7-ethylenedithiocholest-5-ene (CXV) (1.6 g) as a non-crystallizable semi-solid.

Analysis Found : C, 75.58; H, 10.40  
C₂₉H₄₈S₂ requires: C, 75.65; H, 10.43%  
IR : ν max. 1645 (C=O), 1435, 1225 cm⁻¹ (H₂C-S)  
NMR : δ 5.36s (1H, C6-H), 3.23s (4H, -S-CH₂-CH₂-), 0.96 (Cl0-CH₃), 0.69 (Cl3-CH₃), 0.90 and 0.80 (other methyl protons).
Desulfurization of compound (CXV)

7,7-Ethylenedithiocholest-5-ene (CXV) (0.4 g) and Raney nickel (0.4 g) were taken in absolute ethanol and was refluxed for 20 hr. After filtration, the filtrate was evaporated to dryness. The compound (CXVI) thus obtained was recrystallized from acetone (0.15 g), m.p. 90° (reported m.p. 89.5°), $[\alpha]_D^{25.2} = -56.0°$. This compound (CXVI) was found identical with cholest-5-ene.

Reaction of 3β-acetoxycholest-5-en-7-one (III) with 1,2-ethanedithiol using $\text{BF}_3$-etherate as catalyst

3β-Acetoxycholest-5-en-7-one (III) (2.0 g) in acetic acid (60 ml) was treated with 1,2-ethanedithiol (0.85 g; 9.04 mmol) and freshly distilled $\text{BF}_3$-etherate (2 ml), and the reaction was allowed to stand at room temperature for 1 hr. The solution was diluted with methanol (10 ml), poured into water and extracted with ether. The ethereal layer was washed successively with water, NaHCO$_3$ solution (5%) and water, and dried (Na$_2$SO$_4$). Removal of the solvent yielded 3β-acetoxy-7,7-ethylendithiocholest-5-ene (IV) as a solid, recrystallized from acetonitrile (1.75 g), m.p. 182-184° $[\alpha]_D^{25.2} = -101.26°$.

Analysis Found : C, 71.74; H, 9.60

C$_{31}$H$_{50}$O$_2$S$_2$ requires : C, 71.81; H, 9.65%
Desulfurization of compound (IV)

The dithiolane (IV) (0.5 g) in absolute ethanol (300 ml) was similarly treated with Raney nickel (5 g), which afforded 3β-acetoxycholest-5-ene (CXVII) (0.2 g), m.p. 114° (reported m.p. 116°), [α]D^25 = +80°.

Reaction of 3β-chlorocholest-5-en-7-one (LXX) with 1,2-ethanedithiol using BF₃-etherate as catalyst

The ketone (LXX) (2.0 g) was similarly treated with 1,2-ethanedithiol (0.90 g; 9.57 mmol) in the presence of BF₃-etherate. Usual work up and recrystallization from acetonitrile, afforded 3β-chloro-7,7-ethylenedithiocholest-5-ene (CXVIII) (1.7 g), m.p. 125-126°, [α]D^25 = +120°.

Analysis Found : C, 70.29; H, 9.45
C_{29}H_{47}S_{2}Cl requires : C, 70.34; H, 9.50%

IR : \( \nu_{\text{max}} \) 1645 (C=O), 1430, 1235 \( \text{cm}^{-1} \) (H₂C-S-) and 765 \( \text{cm}^{-1} \) (C-Cl)
Desulfurization of compound CXVIII

The dithiolane (CXVIII) (0.5 g) on desulfurization with Raney nickel (5 g) provided 3β-chlorocholest-5-ene (CXIX), (0.195 g), m.p. 94-95° (reported^81 m.p. 96°), [α]D^25 25°-

Oxidation of dithiolane (CXVIII) with m-chloroperbenzoic acid

The dithiolane (CXVIII) (0.49 g) was dissolved in CH2Cl2 (85 ml) and cooled in ice bath to 10° and stirred. To this m-chloroperbenzoic acid (0.2 g) was added in fractions during 30 min. Stirring was continued for another 2½ hr and complete conversion of starting material was evidenced by TLC which showed single spot. The reaction mixture was worked up in CH2Cl2, washed with 10% solution of sodium bisulfite to destroy unreacted peracid and finally with water and dried (Na2SO4). Removal of the solvent and purification by silica gel column provided 3β-chloro-7,7-ethylenedisulfonylcholest-5-ene (CXX) which was recrystallized from methanol (0.34 g), m.p. 235° (decomposed).

Analysis Found: C, 62.32; H, 8.35

C29H47O4S2Cl requires: C, 62.30; H, 8.41%
I^ •

IR : $\nu_{\text{max.}}$ 1620 (C=C), 1355, 1130 (asymmetric and symmetric stretching of -SO$_2$), 740 (C-Cl), 670 cm$^{-1}$ (C=S).

NMR : δ 5.5s (1H, C6-H), 3.9br,m (1H, C3α-H, W$^\frac{1}{2}$ = 1.2Hz; axial), 3.65br,s (4H, -SO$_2$-CH$_2$CH$_2$-SO$_2$-), 1.11 (C10-CH$_3$), 0.71 (C13-CH$_3$), 0.91 and 0.81 (other methyl protons).

**Reaction of cholest-4-en-3-one (I) with 1,2-ethanediithiol in the presence of BF$_3$-etherate as catalyst**

The ketone (I) (2.0 g) on similar treatment with 1,2-ethanediithiol (0.98 g; 10.42 mmol) gave 3,3-ethylenedithiocholest-4-ene (II) (1.55 g), m.p. 108-110° $\Delta m$+127.4°. Analysis Found : C, 75.63; H, 10.41

C$_{29}$H$_{48}$S$_2$ requires : C, 75.65; H, 10.43%

IR : $\nu_{\text{max.}}$ 1645 (C=C), 1425, 1240 cm$^{-1}$ (H$_2$C=S)

NMR : δ 5.52s (1H, C4-H), 3.2s (4H, 2 x -SCH$_2$), 1.02(C10-CH$_3$), 0.68 (C13-CH$_3$), 0.93 and 0.83 (remaining methyl protons).

**Desulfurization of compound (II)**

The dithiolane (II) (0.3 g) on similar treatment with Raney nickel (4 g) as described earlier, yielded cholest-4-ene (CXXI) (0.105 g), m.p. 77° (reported$^8$ m.p. 79°), $[\alpha]_D^{25.2}+76°$. 

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Oxidation of dithiolane(II) with m-chloroperbenzoic acid

The dithiolane (II) (0.46 g) was dissolved in dichloromethane (80 ml) and treated with m-chloroperbenzoic acid (0.2 g) in the manner as described earlier. Final work up and purification afforded 3,3-ethylenedisulfonylcholest-4-ene (CXXII) which was recrystallized from methanol (0.32 g), m.p. 215° (decomposed).

Analysis Found : C, 66.40; H, 9.13
C₂₉H₄₈O₄S₂ requires : C, 66.41; H, 9.16%

IR : \( \nu_{\text{max.}} \) 1640 (C=C), 1340, 1130 (asymmetric and symmetric stretching of SO₂).

NMR : δ 5.35s (1H, C₄-H), 3.68s (4H, -SO₂-CH₂CH₂-SO₂-), 1.13 (C₁₀-CH₃), 0.76 (C₁₃-CH₃), 0.96 and 0.86 (other methyl protons).

Reaction of 3β-acetoxycholest-5-en-7-one (III) with 2-mercaptoethanol, using BF₃-etherate as catalyst

3β-Acetoxycholest-5-en-7-one (III) (3.5 g) in acetic acid (45 ml) was treated with 2-mercaptoethanol (3.9 g; 50.0 mmol) in the presence of BF₃-etherate (4 ml) as catalyst at room temperature for 30 min. After completion of the reaction, methanol (15 ml) was added. The reaction mixture was poured into water and extracted with ether. The ethereal layer was washed successively with water, NaHCO₃ solution (5%)
and water, and dried (Na$_2$SO$_4$). The oily residue obtained after removal of the solvent was subjected to column chromatography over silica gel. Elution with light petroleum-ether (8:1) gave 3β-(2'-acetoxythioethoxy)cholest-5-en-7-one (CXXIII), recrystallized from methanol (1.5 g), m.p. 88°.

Analysis Found : C, 74.14; H, 9.99

C$_{31}$H$_{50}$O$_3$S requires : C, 74.10; H, 9.96%

IR : $\nu$ max. 1735 (OCOCH$_3$), 1665 (C=O=C=O), 1425, 1245 (H$_2$C=S), 1030 cm$^{-1}$ (C-O)

NMR : δ 5.68s (1H, C6-H), 4.28t (2H, OCH$_2$Ac), 2.82m (3H, C3α-H, -SCH$_2$), 2.05s (3H, -COCH$_3$), 1.16 (C10-C$_3$), 0.69 (C13-C$_3$), 0.92 and 0.82 (other methyl protons).

MS : $M^+$ 502 (8.54, C$_{31}$H$_{50}$O$_3$S), m/z 487 (3.05), 444 (12.2), 443 (37.8), 442 (100; C$_{29}$H$_{46}$O$_8$), 415 (3.66), 414(4.27), 384 (26.83), 383 (93.9), 382 (72.66), 367 (21.95), 329 (7.93), 275 (8.54), 269 (10.97), 234 (12.2), 229 (7.93), 187 (15.85), 175 (15.86), 174 (28.05), 161 (24.4), 159 (10.36), 135 (11.58), 134 (12.2), 109 (7.32), 107 (14.63), 105 (8.54), 95 (10.97), 93 (12.8), 91 (13.41).

Further elution with light petroleum-ether (6:1) afforded 3α-(2'-acetoxythioethoxy)cholest-5-en-7-one (CXXIV) which was recrystallized from methanol (0.9 g), m.p. 82°.
Analysis Found : C, 74.12; H, 9.98

\( C_{31}H_{50}O_3S \) requires : C, 74.10; H, 9.96%

IR : \( \gamma_{\text{max}} \): 1735, 1025 (-OCOCH\(_3\)), 1665 (C=C-C=0), 1430, 1240 cm\(^{-1}\) (H\(_2\)C-S).

NMR : \( \delta \): 5.6s (1H, C6-\( \text{H} \)), 4.3t (2H, -CH\(_2\)-OAc), 3.32m (1H, C3\( \beta \)-\( \text{H} \); \( W_2 = 6\text{Hz}; \) equatorial), 2.84t (2H, -SCH\(_2\)), 2.06s (3H, -OCOCH\(_3\)), 1.18 (C10-CH\(_3\)), 0.68 (C13-CH\(_3\)), 0.91 and 0.81 (other methyl protons).

MS : \( M^+ \): 502 (8.33, \( C_{31}H_{50}O_3S \)), m/z 487 (8.33), 444 (13.3), 443 (33.33), 442 (100, \( C_{29}H_{46}O_3 \)), 415 (5.0), 414 (6.66, 384 (15.0), 383 (60.0), 382 (92.33), 368 (23.33), 367 (70.0), 329 (6.66), 274 (8.33), 269 (20.0), 239 (15.0), 229 (10.0), 227 (11.66), 187 (30.0), 175 (26.66), 174 (80.0), 173 (16.66), 161 (40.0), 159 (20.0), 135 (16.66), 134 (16.66), 109 (10.0), 107 (18.33), 105 (13.33), 95 (16.66), 93 (18.83), 91 (18.33).

Continued elution with light petroleum:ether (4:1)
provided \( 4\alpha-(2'-\text{acetoxythioethoxy})\text{cholest-5-en-7-one (CXXV)} \)
as a non-crystallizable semi-solid (0.5 g).

Analysis Found : C, 74.13; H, 9.98

\( C_{31}H_{50}O_3S \) requires : C, 74.10; H, 9.96%

IR : \( \gamma_{\text{max}} \): 1740, 1030 (-OCOCH\(_3\)), 1665 (C=C-C=0), 1430, 1235 cm\(^{-1}\) (H\(_2\)C-S).
Further elution with light petroleum:ether (1:1) gave 4α-(2'-hydroxythioethoxy)cholest-5-en-7-one (CXXVI) as a semi-solid (0.3 g).

Analysis Found : C, 75.68; H, 10.45

\[ C_{29}H_{48}O_2S \] requires : C, 75.65; H, 10.43%

IR : \( \nu_{\text{max}} \) 3390 (-OH), 1665 (C=O-C=O), 1430, 1240 cm\(^{-1}\) (H\(_2\)C-S).

NMR : \( \delta \) 5.62s (1H, C6-H), 4.1t (2H, -OCH\(_2\)), 3.68t (1H, C4β-H; J = 12Hz; axial), 2.88t (2H, -SCH\(_2\)), 1.16 (C10-CH\(_3\)), 0.67 (C13-CH\(_3\)), 0.91 and 0.81 (other methyl protons).

Acetylation of CXXVI with Ac\(_2\)O-Py

4α-(2'-Hydroxythioethoxy)cholest-5-en-7-one (CXXVI) (0.15 g) was treated with a mixture of pyridine (1 ml) and acetic anhydride (0.6 ml) at room temperature and the reaction mixture was left for 2 hr. Then it was poured into water and extracted with ether. The ethereal layer was washed successively with water, dil. HCl, NaHCO\(_3\) solution (5%) and finally with water, and dried (Na\(_2\)SO\(_4\)). Removal of the solvent gave
4α-(2'-acetoxythioethoxy)cholest-5-en-7-one (CXXV) as a non-crystallizable semi-solid (0.1 g).

**Reaction of 3β-chlorocholest-5-en-7-one (LXX) with 2-mercaptoethanol using BF$_3$-etherate as catalyst**

3β-Chlorocholest-5-en-7-one (LXX) (3.5 g) on similar treatment with 2-mercaptoethanol (3.9 g; 50.0 mmol) afforded compounds CXXIII m.p. 88-89° (1.4 g), CXXIV m.p. 82-83° (0.8 g), CXXV (0.5 g) and CXXVI (0.25 g). These compounds were also obtained earlier in the case of ketone (III).

**Reaction of 3β-chlorocholest-5-en-7-one (LXX) with 3-mercapto-1,2-propanediol in the presence of BF$_3$-etherate as catalyst**

A solution of ketone (LXX) (3.5 g) in acetic acid (100 ml) was treated with 3-mercapto-1,2-propanediol (2.59 g; 23.9 mmol) and freshly distilled BF$_3$-etherate (4 ml), and left at room temperature for 1 hr. The solution was diluted with methanol (15 ml), poured into water and extracted with ether. The ethereal layer was washed successively with water, NaHCO$_3$ solution (5%) water, and dried (Na$_2$SO$_4$). The oily residue obtained after removal of the solvent was subjected to column chromatography over silica gel column. Elution with light petroleum:ether (15:1) gave 3β-(3'-thiohydro-2'-acetoxypropoxy)-7-(5''-acetoxy-1''α,3''β-oxathiane)cholest-5-ene (CXXVII) as a non-crystallizable greenish oil,
Analysis Found : C, 66.84; H, 9.0

C_{37}H_{60}O_6S_2 requires : C, 66.86; H, 9.04%

IR : $\nu_{\text{max}}$ 2560 weak (−SH), 1740 (−OCOCH$_3$), 1420, 1235 (H$_2$C=S), 1045 cm$^{-1}$ (oxathiolane ring)

NMR : δ 5.62s (1H, C6-H), 5.1m (2H, AcO-CH$_2$, AcO-C"H"), 4.25m (4H, C3α-H, -OCH$_2$), 4.0d distorted (1H, oxygen is axially oriented), 2.8m (4H, 2 x -SH$_2$), 2.03s (6H, 2 x -OCOCH$_3$), 1.2 (Cl0-CH$_3$), 0.68 (Cl3-CH$_3$), 0.93 and 0.83 (other methyl protons).

Continued elution with light petroleum:ether (13:1) provided 3β-(3'-thiohydro-2'-acetoxypropoxy)cholesta-5-ene-7-one (CXXVIII) which was recrystallized from methanol (0.45 g) m.p. 122-123°.

Analysis Found : C, 72.16; H, 9.76

C$_{32}$H$_{52}$O$_4$S requires : C, 72.18; H, 9.77%

IR : $\nu_{\text{max}}$ 2565 weak (−SH), 1735(−OCOCH$_3$), 1665 (C=C−C=O), 1420, 1235 (H$_2$C=S) and 1030 cm$^{-1}$ (C=O)

NMR : δ 5.58s (1H, C6-H), 5.1m (1H, AcO-CH), 4.2m (3H, −OCH$_2$, C3α-H), 2.65d (2H, −SCH$_2$), 2.04s (3H, −OCOCH$_3$), 1.18 (Cl0-CH$_3$), 0.67 (Cl3-CH$_3$), 0.91 and 0.81 (other methyl protons).
Further elution with light petroleum:ether (7:1) gave 3β-(3'-hydroxy-2'-acetoxythiopropoxy)cholest-5-en-7-one (CXXIX) as a non-crystallizable oil (0.5 g).

Analysis Found: C, 72.15; H, 9.74
C$_{32}$H$_{52}$O$_4$S requires: C, 72.18; H, 9.77%
IR: $\nu$ max. 3360 (-OH), 1730 (-OOC$_{\text{H}}_3$), 1665 (C=C-C=O), 1425, 1235 (H$_2$C-S) and 1030 cm$^{-1}$ (C-O)
NMR: $\delta$ 5.61s (1H, C6-H), 5.1m (1H, AcO-CH$_3$), 4.22d (2H, -OCH$_2$), 2.90m (3H, -SCH$_2$, C3α-H), 2.05s (3H, -OOC$_{\text{H}}_3$), 1.18 (C10-CH$_3$), 0.67 (C13-CH$_3$), 0.91 and 0.81 (other methyl protons).

Further elution with light petroleum:ether (5:1) provided 3β-(3'-thioacetyl-2'-hydroxypropoxy)cholest-5-en-7-one (CXXX) as a non-crystallizable semi-solid (0.4 g).

Analysis Found: C, 72.15; H, 9.74
C$_{32}$H$_{52}$O$_4$S requires: C, 72.18; H, 9.77%
IR: $\nu$ max. 3390 (-OH), 1740 (-S-C$_{\text{H}}_3$), 1660 (C=C-C=O), 1420, 1235 (H$_2$C-S), 1025 cm$^{-1}$ (C-O)
NMR: $\delta$ 5.61s (1H, C6-H), 3.95m (4H, -OCH$_2$, -OCH$_3$, C3α-H), 3.4d (2H, AcS-CH$_2$), 2.02s (3H, -S-C$_{\text{H}}_3$), 1.2(C10-CH$_3$), 0.67 (C13-CH$_3$), 0.91 and 0.81 (other methyl protons).

Further elution with light petroleum:ether (3:1) gave 3β-(2'-hydroxy-2''-thioacetylisopropoxy)cholest-5-en-7-one (CXXXI) as a non-crystallizable semi-solid (0.35 g).
Analysis Found : C, 72.16; H, 9.75

$C_{32}H_{52}O_4S$ requires : C, 72.18; H, 9.77%

**IR** : $\nu_{\text{max.}}$ 3400 (-OH), 1740 (-SCOCH$_3$), 1660 (C=C-C=O), 1420, 1240 (H$_2$C=S), 1030 cm$^{-1}$ (C-O).

**NMR** : $\delta$ 5.62s (1H, C6-H), 4.27m (4H, -OCH$_2$, -OCH, C3α-H), 3.2d (2H, AcS-CH$_2$), 2.02s (3H, -SCOOCH$_3$), 1.2 (C10-CH$_3$), 0.69 (C13-CH$_3$), 0.92 and 0.82 (other methyl protons).

Elution with light petroleum:ether (2:1) provided $4\alpha$-(2'-hydroxy-2''-thioacylisopropoxy)cholest-5-en-7-one (CXXXII) as a semi-solid (0.25 g).

Analysis Found : C, 72.16; H, 9.80

$C_{32}H_{52}O_4S$ requires : C, 72.18; H, 9.77%

**IR** : $\nu_{\text{max.}}$ 3360 (-OH), 1735 (-SCOCH$_3$), 1660 (C=C-C=O), 1420, 1230 (H$_2$C=S), 1030 cm$^{-1}$ (C-O)

**NMR** : $\delta$ 5.67s (1H, C6-H), 4.32m (4H, -OCH$_2$, -OCH, C4β-H), 3.5d (2H, AcS-CH$_2$), 2.01s (3H, -SCOOCH$_3$), 1.16 (C10-CH$_3$), 0.69 (C13-CH$_3$), 0.93 and 0.83 (other methyl protons).

Further elution with light petroleum:ether (1:1) gave $4\alpha$-(3'-acetoxy-2'-hydroxythiopropoxy)cholest-5-en-7-one(CXXXIII) as a non-crystallizable semi-solid (0.3 g).

Analysis Found : C, 72.14; H, 9.76

$C_{32}H_{52}O_4S$ requires : C, 72.18; H, 9.77%
IR : \( \nu_{\text{max}} \) 3360 (-OH), 1730 (-OCOCH\(_3\)), 1660 (C=C-C=O), 1415, 1230 (H\(_2\)C-S), 1030 cm\(^{-1}\) (C-O)

NMR : \( \delta \) 5.65s (1H, C6-H), 5.1d (2H, AcO-CH\(_2\)), 4.3m(1H, -OCH), 2.85m (3H, -SCH\(_2\), C4\(\beta\)-H), 2.05s (3H, -OCOCH\(_3\)), 1.18 (C10-CH\(_3\)), 0.68 (C13-CH\(_3\)), 0.92 and 0.82 (other methyl protons).

**Acetylation of compounds CXXIX-CXXXIII**

The compound (CXXIX) (0.15 g) was treated with a mixture of pyridine (1 ml) and acetic anhydride (0.6 ml) and the reaction mixture was left overnight. Then it was poured into water and extracted with ether. The ethereal layer was washed successively with water, dil. HCl, NaHCO\(_3\) solution (5\%) and finally with water, and dried (Na\(_2\)SO\(_4\)). Removal of the solvent gave 3\(\beta\)-(3',2'-diacetoxythiopropoxy)cholest-5-en-7-one(CXXXIV) as a semi-solid (0.105 g).

Analysis Found : C, 71.06; H, 9.37

C\(_{34}\)H\(_{54}\)O\(_5\)S requires : C, 71.08; H, 9.41\%

IR : \( \nu_{\text{max}} \) 1735 (-OCOCH\(_3\)), 1665 (C=C-C=O), 1425, 1230 (H\(_2\)C-S), 1030 cm\(^{-1}\) (C-O).

NMR : \( \delta \) 5.62s (1H, C6-H), 5.2m (3H, AcO-CH\(_2\), AcO-CH\(_2\)), 2.95m (3H, -SCH\(_2\), C3\(\alpha\)-H), 2.05 (6H, 2 x -OCOCH\(_3\)), 1.2 (C10-CH\(_3\)), 0.69 (C13-CH\(_3\)), 0.93 and 0.83 (other methyl protons).
Acetylation of CXXX

On similar treatment, compound (CXXX) (0.1 g) with acetic anhydride-pyridine afforded 3β-(3'-thioacetyl-2'-acetoxypropoxy)cholest-5-en-7-one (CXXXV) as a semi-solid (0.06 g).

Analysis Found : C, 71.06; H, 9.40
C_{34}H_{54}O_{5}S requires : C, 71.08; H, 9.41%
IR : \( \nu \) \text{max.} 1735 (\text{-SCOCH}_3, \text{-OCOCH}_3), 1665 (C=C-C=0),
1420, 1235 (H_2C=S), 1030 cm\(^{-1}\) (C-O).
NMR : \( \delta \) 5.65s (1H, C6-H), 5.0m (1H, AcO-CH), 4.1m (3H, -OCH\(_2\), C3α-H), 3.35d (2H, AcS-CH\(_2\)), 2.03s (6H, -OCOCH\(_3\), -SCOCH\(_3\)), 1.2 (Cl0-CH\(_3\)), 0.69 (Cl3-CH\(_3\)), 0.93 and 0.83 (other methyl protons).

Acetylation of CXXXI

The compound (CXXXI) (0.1 g) on similar treatment with acetic anhydride-pyridine provided 3β-(2'-acetoxy-2''-thioacetylisopropoxy)cholest-5-en-7-one (CXXXVI) as a non-crystallizable semi-solid (0.65 g).

Analysis Found : C, 71.05; H, 9.40
C_{34}H_{54}O_{5}S requires : C, 71.08; H, 9.41%
IR : \( \nu \) \text{max.} 1735 (\text{-SCOCH}_3, \text{-OCOCH}_3), 1660 (C=C-C=0),
1420, 1230 (H_2C=S), 1030 cm\(^{-1}\) (C-O).
NMR : \( \delta \) 5.65s (1H, C6-H), 5.1d (2H, AcO-CH\(_2\)), 4.28m (2H, -OCH\(_2\), C3α-H), 3.2d (AcS-CH\(_2\)), 1.18(Cl0-CH\(_3\)), 0.69 (Cl3-CH\(_3\)),
0.93 and 0.83 (other methyl protons).

**Acetylation of CXXXII**

Acetylation of compound (CXXXII) (0.09 g) with acetic anhydride-pyridine provided 4α-(2'-acetoxy-2"-thioacetyl-isoproxy)cholest-5-en-7-one (CXXXVII) as a semi-solid (0.05 g).

Analysis Found : C, 71.01; H, 9.38

C₃₄H₅₄O₅S requires : C, 71.00; H, 9.41%

IR : \( \nu_{\text{max.}} 1735 (-\text{SCOCH₃}, -\text{OCOCH₃}), 1660 (\text{C=C-C=O}), 1420, 1235 (\text{H₂C-S}), 1030 \text{ cm}^{-1} (\text{C-O}). \)

NMR : δ5.68s (1H, C6-\( \delta \)), 5.1d (2H, AcO-\( \delta \)), 4.28m (2H, -OCH, C4β-\( \delta \)), 3.45d (2H, AcS-\( \delta \)), 2.03s (6H, -OCOCH₃, -SCOCH₃), 1.2 (C10-\( \delta \)), 0.69 (C13-\( \delta \)), 0.94 and 0.84 (other methyl protons).

**Acetylation of CXXXIII**

The compound (CXXXIII) (0.1 g) on similar treatment with acetic anhydride-pyridine afforded 4α-(3',2'-diacetoxythio-propoxy)cholest-5-en-7-one (CXXXVIII) as a non-crystallizable semi-solid (0.075 g).

Analysis Found : C, 71.05; H, 9.39

C₃₄H₅₄O₅S requires : C, 71.08; H, 9.41%

IR : \( \nu_{\text{max.}} 1730 (-\text{OCOCH₃}), 1660 (\text{C=C-C=O}), 1420, 1235 (\text{H₂C-S}), 1030 \text{ cm}^{-1} (\text{C-O}). \)
NMR : δ 5.68s (1H, C6-H), 5.15m (3H, AcO-CH₂, AcO-CH), 2.8m (3H, -SCH₂, C4β-H), 2.05s (6H, 2 x -OCOCH₃), 1.18 (Cl0-CH₃), 0.69 (Cl3-CH₃), 0.93 and 0.83 (other methyl protons).

Reaction of 3β-acetoxycholesterol-5-en-7-one (III) with 3-mercaptopropan-1,2-diol using BF₃-etherate as catalyst

3β-Acetoxycholesterol-5-en-7-one (III) (3.0 g) was similarly treated with 3-mercaptopropan-1,2-diol (2.22 g; 20.55 mmol) in the presence of acetic acid and BF₃-etherate. After completion of the reaction, the reaction mixture was usually worked up and subjected to the column chromatography over silica gel column. The elution with light petroleum:ether (13:1) provided 3β-(3'-thiohydro-2'-acetoxypropoxy)cholesterol-5-en-7-one (CXXVIII) which was recrystallized from methanol (1.1 g), m.p. 122-123°. This compound was also obtained earlier in the case of ketone LXX.

Further elution with light petroleum:ether (6:1) afforded 3β-(3'-acetoxy-2'-hydroxythiopropoxy)cholesterol-5-en-7-one (CXXXIX) which was recrystallized from methanol (1.35 g), m.p. 134-135°.

Analysis Found : C, 72.13; H, 9.72
C₅₂H₅₂O₄S requires : C, 72.18; H, 9.77%
IR : $\nu_{\text{max}}$, 3400 (-OH), 1735 (OOCCH$_3$), 1665 (C=C=C=O), 1420, 1235 (H$_2$C=S), 1030 cm$^{-1}$ (C-O).

NMR : $\delta$ 5.59s (1H, C6-H), 5.0d (2H, AcO-CH$_2$), 4.1m (1H, -OCH$_3$), 2.85m (3H, -SCH$_2$, C3a-H), 2.04s (3H, -OOCCH$_3$), 1.16 (C10-CH$_3$), 0.67 (C13-CH$_3$), 0.91 and 0.81 (other methyl protons).

**Acetylation of CXXXIX**

The compound (CXXXIX) (0.2 g) on treatment with acetic anhydride (0.8 ml) and pyridine (1.2 ml) gave 3\$-(3',2'-diacetoxythiopropoxy)cholestan-5-en-7-one (CXXXIV) (0.17 g) as a semi-solid. The same compound (CXXXIV) was also obtained earlier on acetylation of compound (CXXIX) with acetic anhydride-pyridine.
References


56. K. Igarashi (Japan Patent) 8,076 (1957); Chem. Abst., 52, 13808i (1958).


80. J. Mauthner, Monatsch, 30, 635 (1909).


88. J. Mauthner, Monatsch, 28, 1113 (1907).
Part One

B. Bamford-Stevens Reaction
Bamford and Stevens\(^1\) reported the alkaline decomposition of a number of p-toluenesulfonylhydrazones. This reaction, now known as Bamford–Stevens reaction, is noted for giving rise to a variety of products. The tosylhydrazones of aromatic aldehydes and ketones gave aryl diazomethanes\(^1,2\) whereas, aliphatic and alicyclic analogues gave olefins, sometimes olefin formation is accompanied with the skeletal rearrangement. Diazonium compound has been suggested as an intermediate in the latter case. Hydrocarbons, azines, triazoles and ethers have also been reported as Bamford–Stevens reaction products.

Pinacolone tosylhydrazone (I) on alkaline decomposition in the protic solvent gave tetramethylethylene (II).

\[
\text{(CH}_3\text{)}_2\text{C}^\text{=C}=\text{NNH-Ts} \quad \xrightarrow{\text{Na; Ethylene glycol}} \quad \text{(II)}
\]
Djerassi et al.\textsuperscript{3} subjected 2α-methylcholestan-3-one tosylhydrazone (III) on alkaline decomposition and reported the formation of 2-methylcholest-2-ene (IV).

Barton and Robinson\textsuperscript{4} subjected some steroidal p-toluene-sulfonylhydrazones to Bamford-Stevens reaction and obtained olefinic compounds. Cholestan-6-one tosylhydrazone (V) on treatment with sodium in ethylene glycol yielded cholest-5-ene (VI).
3β-Acetoxyergost-22-en-6-one tosylhydrazone (VII) and 3β-acetoxyergosta-7,22-dien-6-one tosylhydrazone (IX) on treatment with sodium in ethylene glycol under the same reaction conditions yielded 3β-acetoxyergosta-5,22-diene (VIII) and ergosteryl acetate (X) respectively.

\[
\begin{align*}
\text{AcO} & \quad \text{Na} \\
(\text{VII}) & \quad \text{Ethylene glycol} & (\text{VIII})
\end{align*}
\]

Corey and Sneen treated 3β-hydroxycholestan-7-one tosylhydrazone (XI) with sodium in ethylene glycol to get 3β-hydroxycholesterol-7-ene (XII).

\[
\begin{align*}
\text{AcO} & \quad \text{NNH-Ts} \\
(\text{IX}) & \quad \text{"} & (\text{X})
\end{align*}
\]
Elks et al.\textsuperscript{6} carried out the decomposition of hecogenin acetate tosylhydrazone (XIII) with sodium in ethylene glycol and obtained products (XIV), (XV) and (XVI).
The decomposition of tosylhydrazone (XVII) of estrone methyl ether, catalyzed by a base, in which the migration of a methyl group took place, has been reported by Johns.

\[
\text{(XVII)} \quad \xrightarrow{\text{NNH-Ts}} \quad \text{(XVIII)} + \text{(XIX)}
\]

When 3β,20β-dihydroxy-5α-pregn-12-one tosylhydrazone (XX) was subjected to pyrolytic decomposition with sodium in ethylene glycol, it gave (XXI)\(^8\). The structure of XXI has been modified\(^9\) to XXII.
Dannenberg and Gross\textsuperscript{10} reported the aromatization of ring A by alkaline decomposition of cholesta-1,4-dien-3-one tosylhydrazone (XXIII).

The tosylhydrazones (XXVI) and (XXVIII) gave ethers (XXVII) and (XXIX) respectively when heated with sodium in ethylene glycol\textsuperscript{1,11}. 

(XXII)
PhCH=NNHTs $\xrightarrow{\text{Na, Ethylene glycol}} [\text{PhCH=N}_2]$ $\xrightarrow{\Delta} \text{PhCH}_2\text{OCH}_2\text{CH}_2\text{OH}$  

(XXVI)  

(Ph)$_2$C=NNHTs $\xrightarrow{\text{Na, Ethylene glycol}} [(\text{Ph})_2\text{C=N}_2]$ $\xrightarrow{} (\text{Ph})_2\text{CHOCH}_2\text{CH}_2\text{OH}$  

(XXVIII)  

(XXIX)  

The products obtained, in Bamford-Stevens reaction, depend upon the nature of solvent used. The decomposition of tosylhydrazones in different solvents e.g. protic and aprotic has been reported$^{12-14}$. The camphor tosylhydrazone (XXX) on decomposition in protic solvent yielded camphene (XXXI). When aprotic solvent was used, the tricyclene$^{12-14}$ was formed as the major product.

(XXX)  

(XXXI)  

The effect of solvents on such process was also indicated by the reaction of 2—methylpropanal tosylhydrazone and sodium methoxide in diethylene glycol which gave 2-methylpropene (65%), cis-2-butene (4%), trans-2-butene (8%), 1-butene (10%) and methylcyclopropane (12%) whereas, in diethyl carbitol,
2-methylpropene (64%) and methylcyclopropane (36%) were formed in 80% yield\textsuperscript{12}. The reaction of 2-methylpropanal tosylhydrazone suggested the formation of its salts and methanol; its thermal decomposition in diethyl carbitol gave 2-methylpropene (62%) and methylcyclopropane (37%)\textsuperscript{12}.

Friedman and Shechter\textsuperscript{12} suggested that the salts of tosylhydrazones decompose to diazo compounds and these diazo compounds undergo (i) proton transfer from donor solvents and cationic decomposition of Wagner-Meerwein type involving hydrogen and carbon skeleton rearrangement (ii) carbenic decomposition in aprotic solvents to give olefins by hydrogen migration.

\[ \begin{align*}
\text{R} & \quad \text{C=N-NHTs} \quad \xrightarrow{\text{Base}} \quad \text{R} \quad \text{C=N-NTs} \\
\text{R} & \quad \text{R} \quad \text{R} \quad \text{R} \\
\text{R} & \quad \text{C=N\textsuperscript{+}N Ts} \quad \xrightarrow{\text{Heat}} \quad \text{R} \quad \text{C=N=N + (p) CH\textsubscript{3}C\textsubscript{6}H\textsubscript{4}SO\textsubscript{2}} \\
\text{R} & \quad \text{R} \quad \text{R} \quad \text{R} \\
\text{R} & \quad \text{C=N\textsuperscript{+}N} \quad \xrightarrow{\text{Protic solvent}} \quad \text{R} \quad \text{CH-N\equiv N} \quad \xrightarrow{\text{(i)}} \quad \text{R} \quad \text{CH} \\
\text{R} & \quad \text{R} \quad \text{R} \quad \text{R} \\
\text{R} & \quad \text{C=N\textsuperscript{+}N} \quad \xrightarrow{\text{Aprotic solvent}} \quad \text{R} \quad \text{C:} \\
\text{R} & \quad \text{R} \quad \text{R} \quad \text{R}
\end{align*} \]
The additional evidence for the carbenic process has been derived from the thermal decomposition of 1-diazo-2-methylpropane which yields 2-methylpropane (67%) and cyclopropene. The generation of carbenes when it is carried out in aprotic solvents has also been reported by Cristol and Harrington. DePuy and Froemsdorf reported that in the base catalyzed decomposition of tosylhydrazone, olefins are formed according to the Saytzeff's rule i.e. the more substituted olefins are formed in major amount. Thus the product from the elimination of the tosylhydrazone (XXXII) of 2-butanone contain 2-butenes (67%) and 1-butene (28%).

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{C} & \equiv \text{CH}_3 \\
\text{NNHTs} & \rightarrow \text{CH}_3\text{CH}_2\text{CH} = \text{CH}_2 \quad (28\%) \\
+ \\
\text{CH}_3 & \text{C} = \text{C} \quad \text{H} \\
\text{H} & \text{C} = \text{C} \quad \text{CH}_3 \\
(37\%) \\
+ \\
\text{CH}_3 & \text{C} = \text{O} \quad \text{CH}_3 \\
\text{H} & \text{H} \\
(30\%) \\
+ \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3 & \quad (5\%)
\end{align*}
\]
Bamford-Stevens reaction is important in the sense that it gives rise to a variety of compounds, notable amongst them are olefins with or without skeletal rearrangement, others, azines and saturated hydrocarbons. Formation of different products on alkaline decomposition of tosylhydrazones of ketones including saturated steroidal ketones have been reported earlier. When 3β-acetox-5α-cholestan-6-one tosylhydrazone (XXXIII) was subjected to Bamford-Stevens reaction followed by acetylation it gave cholesteryl acetate (XXXIV), 3β-acetox-5α-cholestan-6α-yl,2'-acetoxyethyl ether (XXXVa) and 3β-acetox-5α-cholestan-6α-yl,2'-hydroxyethyl ether (XXXVb)\(^{17}\).
The present work describes the similar decomposition of tosylhydrazone of an α,β-unsaturated steroidal ketone, namely 3β-acetoxycholest-5-en-7-one (XXXVI).

\[ \text{AcO(XXXVI)} \]

**Reaction of 3β-acetoxycholest-5-en-7-one (XXXVI) with p-toluenesulfonylhydrazide**

The ketone (XXXVI) was treated with p-toluenesulfonylhydrazide in acetic acid and kept overnight at room temperature. The solid thus obtained was recrystallized from methanol which provided a compound, m.p. 158-159°.

\[ \text{(XXXVI)} \rightarrow \text{(XXXVII)} \]
Characterization of the compound, m.p. 158-159° as 3β-acetoxycholest-5-en-7-one tosylhydrazone (XXXVII)

Elemental analysis of compound (XXXVII) showed the composition $C_{36}H_{54}N_{2}O_{4}S$, which clearly indicated the formation of tosylhydrazone. Its IR spectrum exhibited bands at 1735 (-O-COCH$_3$), 1645 (C=N), 1610 (-C=C-) and 1030 cm$^{-1}$ (-O-C-)\(^\text{18}\). The NMR spectrum showed a doublet at δ 7.32 for two aromatic protons (C2-H and C6-H; J = 9Hz), another doublet at 7.2 for another set of two aromatic protons (C3-H and C5-H; J = 9Hz), a sharp singlet at 5.7 for one C-6 vinylic proton, a broad multiplet centred at 4.66 ($W_\nu = 18$Hz; axial)\(^\text{19}\) which was ascribable to C3β-H and another sharp singlet at 2.02 for acetoxy group protons. The methyl protons appeared at δ 1.04 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.92 and 0.80 (other methyl protons). On the basis of foregoing discussion the compound having m.p. 158-159° may be regarded as 3β-acetoxycholest-5-en-7-one tosylhydrazone (XXXVII).

Reaction of 3β-acetoxycholest-5-en-7-one tosylhydrazone (XXXVII) with sodium-ethylene glycol

The tosylhydrazone (XXXVII) was subjected to sodium-ethylene glycol decomposition at 150°. The crude product thus obtained was acetylated with acetic anhydride-pyridine mixture. After usual work up and chromatography over neutral alumina column, a compound having m.p. 82° was obtained.
Characterization of the compound, m.p. 82° as 7α-(2′-hydroxyethoxy)cholest-5-en-2′,3-diacetate (XXXVIII)

The compound having m.p. 82° was analyzed correctly for \( C_{33}H_{54}O_{5} \). Its IR spectrum showed characteristic strong bands at 1745 (–OOCCH\(_3\)\( ^\)\( ^\)\), 1660 (C=C–C–O–) and 1030 cm\(^{-1}\) (C–O). The NMR spectrum showed a doublet at \( \delta 5.6 \) for C-6 vinylic proton \( (J = 2.8\text{Hz}) \), a broad multiplet at 4.64 for C3α-H \( (W^\perp = 18\text{Hz}; \) axial)\( ^\)\( ^\)\), a one proton triplet at 4.22 (C7β-H), a quartet centred at 3.70 which can be assigned to methylene protons \( \alpha \)-to the acetoxy group (AcO-CH\(_2\)-) and another quartet for two protons at 3.51 (–OCH\(_2\)\( ^\)\( ^\)\), Two sharp singlets each for three protons were observed at \( \delta 2.06 (\text{CH}_2\text{OOCCH}_3) \) and \( 2.01 (\text{C}_3\text{OOCCH}_3) \). The methyl signals were seen at \( \delta 1.02 (\text{Cl0-CH}_3), 0.68 (\text{Cl3-CH}_3), 0.91 \) and 0.81 (for remaining methyl protons). Thus on the basis of above data the compound having m.p. 82° was characterized as 7α-(2′-hydroxyethoxy) cholest-5-en-2′,3-diacetate (XXXVIII).
Experimental

All melting points were observed on a Kofler apparatus and are uncorrected. Infrared (IR) spectra were recorded in Nujol with a Perkin-Elmer 237 spectrophotometer. IR values are given in cm\(^{-1}\). Nuclear magnetic resonance (NMR) spectra were run in CDCl\(_3\) on a Varian A60 instrument with tetramethylsilane (TMS) as internal standard and its values are given in ppm (\(\delta\)). Thin layer chromatographic (TLC) plates were coated with silica gel G and sprayed with 20\% aqueous solution of perchloric acid. Light petroleum refers to a fraction b.p. 60-80°. Anhydrous sodium sulfate (Na\(_2\)SO\(_4\)) was used as the drying agent. The abbreviations "s,d,t,q,m and br" denote "singlet, doublet, triplet, quartet, multiplet and broad", respectively.

3\(\beta\)-Acetoxycholest-5-en-7-one tosylhydrazone (XXXVII)

3\(\beta\)-Acetoxycholest-5-en-7-one (XXXVI) (2.5 g) was dissolved in warm glacial acetic acid (30 ml). The solution was cooled, p-toluenesulfonylhydrazide (2.5 g) was added with shaking and kept overnight at room temperature. The solid thus obtained was filtered, washed with ethanol and dried (Na\(_2\)SO\(_4\)). Recrystallization from methanol gave tosylhydrazone (XXXVII) (1.2 g), m.p. 158-159°.
Analysis Found : C, 70.80; H, 8.83; N, 4.56

\[ \text{C}_3\text{H}_5\text{N}_2\text{O}_4 \text{ requires : C, 70.81; H, 8.85; N, 4.59%} \]

IR : \( \nu_{\text{max}} \) 1735 (C=O), 1645 (C=N), 1610 (C=C), 1030 cm\(^{-1}\) (C-O).

NMR : \( \delta \) 7.32d (2H, C'2-H, C'6-H; J = 9Hz), 7.2d (2H, C'3-H, C'5-H; J = 9Hz), 5.7s (1H, C6-H), 4.66m (1H, C3α-H, \( W_\perp = 18\)Hz, axial), 2.02s (CH₃CO-), 1.04 (ClO-CH₃), 0.68 (Cl3-CH₃), 0.92 and 0.80 (other methyl protons).

Alkaline decomposition of tosylhydrozone (XXXVII)

The tosylhydrazone (XXXVII) (1.0 g) was suspended in a solution prepared by dissolving sodium (2.5 g) in ethylene glycol (25 ml) and the mixture was heated on an oil bath for 2 hr at 150°C. After cooling to room temperature, the reaction mixture was poured into ice cooled water and extracted with ether. The ethereal layer was washed with water, dil. HCl, sodium bicarbonate solution (5%) and finally with water, and dried (Na₂SO₄). Removal of the solvent gave an oil (1.3 g) which was treated with acetic anhydride (1.5 ml) and pyridine (2.5 ml). The reaction mixture was left overnight and then heated on water bath for 1 hr. It was poured into ice-cooled water and extracted with ether. The ethereal layer was washed with water, dil. HCl, sodium bicarbonate solution (5%) and finally with water, and dried (Na₂SO₄). Removal of the solvent gave an oil (0.73 g) which was chromatographed over neutral alumina. Elution with light petroleum:ether (4:1) gave
7α-(2'-hydroxyethoxy)cholest-5-en-2',3-diacetate (XXXVIII), recrystallized from methanol (0.43 g), m.p. 82°.

Analysis Found : C, 74.70; H, 10.10.
C_{33}H_{54}O_{5} requires : C, 74.71; H, 10.18%

IR : \( \nu_{\text{max}} \) 1745 (-OCOCH₃), 1660 (C=C-C=O-), 1245, 1030 cm⁻¹ (C-O)

NMR : δ 5.6d (1H, C6-H, J = 2.8Hz), 4.64br, m (1H, C3α-H; \( \nu \) = 18Hz, axial), 4.22t (1H, C7-βH), 3.7q (2H, CH₂OAc), 3.51q (2H, -OCH₂), 2.06s (3H, -OCH₃), 2.01s (3H, C3-OCOCH₃), 1.02 (3H, -CH₃), 0.68 (3H, -CH₃), 0.91 and 0.81 (other methyl protons).
References

