STEROIDAL REACTIONS

RESUME

THESIS SUBMITTED FOR THE DEGREE OF
Doctor of Philosophy
IN
CHEMISTRY

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This is to certify that the work embodied in this thesis entitled "Steroidal Reactions" is the original work done by Mr. Rajesh Kumar Pathak under my supervision. The thesis is suitable for submission for the award of the degree of Doctor of Philosophy in Chemistry.
To My
GRAND PARENTS
Acknowledgments

I wish to express my deep sense of gratitude to Prof. Shafiullah, Department of Chemistry, for his able guidance and constant encouragement throughout the tenure of research work. I am highly indebted to Dr. M. Mushfiq Reader, for his keen interest and generous help, I am also thankful to Prof. M.S. Ahmad, former chairman, for useful discussion and Prof. S.A.A. Zaidi, Chairman, Department of Chemistry, A.M.U., Aligarh, for providing necessary facilities.

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RAJESH KUMAR PATHAK
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Summary

The chemistry of steroids became a matter of paramount interest in recent past because of their immense use in research and industry owing to their broad spectrum of biological properties. In this thesis the syntheses of some important hetero-steroids are described. The products obtained are characterized on the basis of spectral studies and chemical transformations. The results are summarized as below:

CHAPTER - ONE

SYNTHESSES OF STEROIDAL OXOSPIROTHIAZOLOTETRAZINES

Syntheses and biological activities of steroidal compounds having heterocyclic ring systems and containing spiro linkage have been reported in the literature. This prompted us to undertake the reaction of steroidal-6-ketones, with thiocarbohydrazide in dry ethanol and acetic acid to obtain steroidal spirotetrazine-thiones (VI - X)^a as the products which were further refluxed with chloroacetic acid and sodium acetate in dry ethanol and gave oxospirothiazolotetrazines (XI - XV)^b.

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SYNTHESSES OF OXAZETENE

Various oxygen and nitrogen containing steroidal compounds have been reported in the literature with their biological importance. We carried out the reaction of steroidal hydroxy ketones (XVI - XVIII) with benzoic hydrazide in ethanol and obtained steroidal [6,5-c]-oxazetenes (XIX - XXI) as the products containing nitrogen and oxygen heterocyclic ring system.
A - SYNTHESSES OF STEROIDAL THIOCARBOXYLIC KETOXIME ANHYDRIDES

The synthesis of cholest-4-ene-4-thiocarboxylic-6-keto-ketoxime anhydride (XXV), its 3β-acetoxy (XXVI) and 3β-chloro (XXVII) analogues from the corresponding steroidal nitro-olefins (XXII - XXIV) is described.

Recently Barton and coworkers have reported a mild procedure for the reduction of aliphatic nitro compounds to oximes in which they used carbon disulphide in the presence of triethylamine. We have also followed the same procedure with some steroidal nitro olefins (XXII - XXIV), in anticipation of obtaining the corresponding oximes which could be further utilized for Beckmann rearrangement.
Surprisingly enough, in place of oximes cyclic thiocarboxylic ketoxime anhydrides (XXV - XXVII) were obtained as the products (XXV - XXVII).

B - SYNTHESSES OF STEROIDAL OXATHIOLANE THIONE

In recent years the chemistry of organic heterocyclic compounds has become the major area of research for organic chemists. The biological and pharmacological activities exhibited by such compounds have drawn their attention and the syntheses of a large number of sulphur containing heterocyclic compounds have been reported. Alongwith the similar lines syntheses of steroidal

oxathiolane thione has been undertaken in this study. The reaction of 5,6α-epoxy-5α-cholestan (XXVIII) with carbon-disulphide in the presence of triethylamine at room temperature afforded 5α-cholestan[6α,5-d]-1',3'-oxathiolane-2'-thione (XXXII). Under similar reaction conditions its 3β-hydroxy (XXIX), 3β-acetoxy (XXX) and 3β-chloro (XXXI) analogues gave 3β-hydroxy-5α-cholestan[6α,5-d]-1',3'-oxathiolane-2'-thione (XXXIII), 3β-acetoxy-5α-cholestan[6α,5-d]-1',3'-oxathiolane-2'-thione (XXXIV) and 3β-chloro-5α-cholestan[6α,5-d]-1',3'-oxathiolane-2'-thione (XXXV) as the products respectively.

d. Synthesis of steroidal oxathiolane thiones.
Acta Chimica Hungarica ------- (In press).
Lead tetraacetate (LTA) has been proved to be a useful and versatile reagent in organic chemistry. Many interesting results of its reactions with a variety of organic substrates have been observed. In addition to its utility in cleaving diols and in oxidizing alcohols lead (IV) acetate may also be used to introduce acetoxy group in steroidal compounds at their activated positions. The oxido steroids are also formed by the reaction of lead (IV) acetate. Many workers have reported oxido steroids from epoxides and bromohydrin but no oxido steroid has been reported by the reaction of lead (IV) acetate with steroidal diols so far. This prompted us to work on the reactions of steroidal diols, epoxides and hydroxyketoximes with lead (IV) acetate.

**REACTIONS OF STERoidal DIOLS WITH LEAD (IV) ACETATE**

The reaction of 3β-chloro-5,6β-dihydroxy-5α-cholestane (XXXVI) with lead (IV) acetate in dry benzene and a catalytic amount of iodine under reflux afforded 3β-chloro-6β,19-oxido-5-hydroxy-5α-cholestane(XXXIX). Under similar reaction conditions, its 3β-acetoxy (XXXVII) and 3β-hydroxy(XXXVIII) analogues gave 3β-acetoxy-6β,19-oxido-5-hydroxy-5α-cholestane (XL) and 3β,5-
dihydroxy-6β,19-oxido-5-hydroxy-5α-cholestan (XLI), respectively.

Reaction of steroidal epoxides with lead (IV) acetate

Reaction of 5,6α-epoxy-5α-cholestan (XXVIII) and its 3β-chloro analogue (XXXI) with lead (IV) acetate in glacial acetic acid furnished 5-hydroxy-6β-acetoxy-5α-cholestan (XLII), 5,6β-di-acetoxy-5α-cholestan (XLIV), 3β-chloro-5-hydroxy-6β-acetoxy-5α-cholestan (XLIII) and 3β-chloro-5,6β-diacetoxy-5α-cholestan (XLV), respectively while 3β-acetoxycholest-5-ene (XLVI) and 3β,5-diacetoxy-6β-hydroxy-5α.cholestan (XLVII) were obtained as the products with the reactions of 3β-hydroxy-5,6α-epoxy-5α-cholestan (XXIX) and its 3β-acetoxy derivative (XXX) with lead.

e. Synthesis of 6β,19-oxidosteroids.
(IV) acetate in glacial acetic acid. 

\[ \text{Pb(OAc)}_4 \text{AcOH, AcOK Reflux, 8 hrs} \]

\[ \text{R} \]

(XXVIII) H

(XXXI) Cl

(XXIX) OH

(XXX) OAc

(XLII) H

(XLIII) Cl

(XLIV) H

(XLV) Cl

(XLVI)

(XLVII)

---

f. Reaction of lead (IV) acetate with steroidal epoxides. 
REACTION OF STEROIDAL HYDROXY KETOXIMES WITH LEAD (IV) ACETATE

Reaction of 3β,5-dihydroxy-5α-cholestan-6-one oxime (XLVIII) and its 3β-acetoxy derivative (L) in dry benzene with lead (IV) acetate gave 3β-acetoxycholest-4-en-6-one (LI), 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (LIII), 3β,5-dihydroxy-5α-cholestan-6-N-acyloxime(LIV) and 3β-acetoxy-5-hydroxy-5α-cholestan-6-N-acyl oxime (LVI). Under similar reaction conditions 3β-chloro-5-hydroxy-5α-cholestan-6-one oxime(XLIX) provided 3β-chlorocholest-4-en-6-one (LII), 3β-chloro-5-hydroxy-5α-cholestan-6-N-acyl oxime (LV) and 3β-chloro-7α-acetoxy-5-hydroxy-5α-cholestan-6-one (LVII)\(^g\).

\[ \text{Pb(OAc)}_4 \text{ Dry Benzene r.t. 2 hrs} \]

\begin{align*}
\text{R} & \quad \text{OH} \\
\text{R} & \quad \text{OAc} \\
\text{R} & \quad \text{Cl}
\end{align*}

\[ g. \quad \text{Lead (IV) acetate oxidation of steroidal hydroxy ketoximes.} \]
\[ \text{J. Ind. Chem. Soc., Ms. No. 573/89 -- (Communicated for publication).} \]
Basic alumina has been successfully employed for the preparation of dienoic esters from \( \beta \)-allenic esters in good yield with high stereospecificity. Alumina being an adsorbent provides a reaction site for various interesting transformations. Alumina also provides reactive surface for the chromatographic conversions. These characteristics of alumina have been exploited here for solid phase syntheses of steroidal olefins and steroidal nitroolefins.
SYNTHESIS OF 6-NITROCHOLESTA-3,5-DIENE (LX ) ON BASIC ALUMINA SURFACE

3β-Hydroxy-6-nitrocholest-5-ene (LVIII) when adsorbed on basic alumina and left at room temperature for 48 hrs a semi solid mass was obtained which on recrystallization from methanol gave 6-nitrocholesta-3,5-diene (LX ). Similarly 3β-acetoxy-6-nitrocholest-5-ene (XXIII) and 3β-tosyloxy-6-nitrocholest-5-ene (LIX) when allowed to stand over a column of basic alumina gave (LX ) as product in quantitative yield, while 3β-chloro-6-nitrocholest-5-ene (XXIV) was eluted unreacted.

\[
\begin{align*}
R & \quad (LVIII) \quad \text{OH} \\
(XXIII) & \quad \text{OAc} \\
(LIX) & \quad \text{OTs} \\
(XXIV) & \quad \text{Cl}
\end{align*}
\]

TRANSFORMATION OF STERoidal EPOXIDES TO OLEFINES OVER NEUTRAL ALUMINA SURFACE

A survey of the literature revealed that methods have been reported for the conversion of steroidal epoxides to olefins but no method was given for the conversion over silver nitrate – neutral alumina surface. So by this method $5,6\alpha$-epoxy-$5\alpha$-cholestane (XXVIII) and its $3\beta$-substituted analogues (XXIX)- XXXI) have been converted to cholest-5-ene (LXI ) and its $3\beta$-substituted olefins (LXII, XLVI andLXIII), respectively).i.

\[ \text{Al}_2\text{O}_3(\text{Neutral}) \rightarrow \text{AgNO}_3 \]

\begin{align*}
\text{R} & \quad \text{R} \\
\text{H} & \quad \text{H} \\
\text{OH} & \quad \text{OH} \\
\text{OAc} & \quad \text{OAc} \\
\text{Cl} & \quad \text{Cl}
\end{align*}

i. A simple method for the transformation of steroidal epoxides to olefins.
Introduction

The explosive growth of natural and synthetic chemistry in the field of steroids during the present century has been the result of concerted efforts of all the leading organic chemists. The problem of isolation of the steroid entities from natural sources, their great value in modern medicine and the interesting pharmacological properties have brought about an increasing interest. The synthetic modification of naturally occurring steroids, with the hope of improving pharmacological essentialities, has resulted in preparation and discovery of a number of diverse pharmacologically active, potent, highly specific commercially important therapeutic agents. The physiological activity of steroidal hormones depends on a number of factors. Among those of primary importance are stereochemistry and overall shape of the molecule. Thus, any really fundamental change (introduction of double bond, hydroxyl group, acetate group and ring enlargement and contraction etc.) in the steroid nucleus should alter the stereochemistry as little as possible. Since these have involved the modification of the basic carbon skeleton of
the steroid nucleus itself, it provided an opportunity to deal with many problems of fundamental organic chemistry such as mechanistic and stereochemical aspects of transformations. Moreover, the deep involvement of modern spectroscopic tools (UV, IR, ¹H-NMR, and mass spectrometry) in the structural elucidation of steroidal compounds is envisaged.

During the last decade the major efforts of the chemists were directed towards modification in the structure of steroids in order to enhance their non-hormonal activity and to increase the selectivity of certain biologically active compounds. The broad spectrum of the biological activities found in these compounds and the multiplicity of action displayed by certain individual members make them one of the most intriguing class of compounds.

Our laboratory, concerned mainly with the syntheses of steroidal compounds and their identification by chemical and spectral studies, has reported the preparation of a number of heterosteroids. In the present work an attempt has been made to synthesize some modified steroids of biological importance. In some cases abnormal products have also been obtained and this has offered scope for some mechanistic and stereochemical studies too.
Part One

Steroidal Oxospirothiazolo Tetrazines and Oxazetenes
Theoretical

In recent past the chemistry of organic heterocycles has become the major area of research for organic chemists. The biological and pharmacological activities such as anesthetic, antiarrhythmic, sedative, antiinflammatory, antimicrobial, analgesic, anticonvulsant, antiulcer, antiviral, antifungal and antihypertensive exhibited by such compounds have drawn their attention and the syntheses of large number of oxygen, nitrogen and sulphur containing heterocyclic compounds have been reported.1-10

The syntheses of a number of steroidal compounds containing heterocyclic rings such as aza and oxa steroids, tetrazoles, oxazoles, thiazoles, aziridines, oxazolines, oxazolidinones, oxazolidinethiones and spirothiazolidinones were reported and some of them found biologically active. Here in an attempt has been made to synthesize steroidal spirotetrazine thiones, oxaspirothiazolotetrazines and oxazetenes. Some of them can be tested for their pharmacological activities.

A number of steroidal as well as non-steroidal ketones condense readily when treated with different reagents under different reaction conditions to provide steroidal nitrogen, oxygen, and sulphur containing heterocycles.
Irmscher\textsuperscript{12} reported the reaction of aminoethanol with 17-hydroxy androstan-6-one (I) in the presence of absolute alcohol and benzene to obtain 17-hydroxy androstan-6-spiro oxaminoethane (II) as a product.

![Reaction Diagram]

Djerassi and coworkers\textsuperscript{13} showed that 2-mercaptoethanol reacts readily in the presence of zinc chloride with unconjugated carbonyl groups to yield corresponding oxathiolanes. Thus androstan-17\textbeta-ol-3-one-17-acetate (III), etiocholan-17\textbeta-ol-3-one-17-acetate (V), estrone (VII) and its acetate (IX), \(\Delta^5\)-androsten-3\textbeta-acetate-17-one (XI), allopregnan-3\textbeta-ol-20-one (XIII) and its 3\textbeta-yl-acetate (XV) as well as \(\Delta^5\)-pregnen-3\textbeta-ol-20-one (XVII) and its 3\textbeta-yl-acetate (XIX) were converted into 5\textalpha-androstan-17\textbeta-ol-3-one-17-acetate-3-ethylene hemithioketal (IV), 5\textbeta-androstan-17\textbeta-ol-3-one-17-acetate-3-ethylene hemithioketal (VI), estrone hydroxy-17-ethylene hemithioketal (VIII), estrone acetate-17-ethylene hemithioketal (X), \(\Delta^5\)-androsten-3\textbeta-acetate-17-one-17-ethylene hemithioketal (XII), \(\Delta^5\)-allo-
pregnen-3β-ol-20-one-20-ethylene hemithioketal (XIV), allo-
pregnan-3β-acetate-20-one-20-ethylene hemithioketal (XVI), 
Δ⁵-pregnen-3β-ol-20-one-20-ethylene hemithioketal (XVIII) and 
Δ⁵-pregnen-3β-acetate-20-one-20-ethylene hemithioketal (XX), 
respectively.
\begin{align*}
&\text{(XI)} \xrightarrow{\begin{array}{c} [\text{SH} ]^\text{OH} \text{ZnCl}_2 \end{array}} \text{(XII)} \\
&\text{(XIII)} \xrightarrow{\begin{array}{c} [\text{SH} ]^\text{OH} \text{ZnCl}_2 \end{array}} \text{(XIV)} \\
&\text{(XV)} \xrightarrow{\begin{array}{c} [\text{SH} ]^\text{OH} \text{ZnCl}_2 \end{array}} \text{(XVI)} \\
&\text{(XVII)} \xrightarrow{\begin{array}{c} [\text{SH} ]^\text{OH} \text{ZnCl}_2 \end{array}} \text{(XVIII)} \\
&\text{(XIX)} \xrightarrow{\begin{array}{c} [\text{SH} ]^\text{OH} \text{ZnCl}_2 \end{array}} \text{(XX)}
\end{align*}
Hauptmann showed the reaction of cholestan-4-en-3-one (XXI) with ethanedithiol, in presence of zinc chloride and sodium acetate and obtained cholest-4-en-3-one-3-ethylene dithiol (XXII) as the product.

\[
\text{C}_{8}H_{17} \quad \text{[SHSH]} \quad \text{ZnCl}_2, \text{Na}_2\text{SO}_4 \quad \rightarrow \quad \text{XXII}
\]

Ralls et al. showed the reaction of ethanedithiol with 3β-acetoxycholesten-5-en-7-one (XXIII) in absolute ether with dry hydrogen chloride as the catalyst and 3β-acetoxy cholesten-5-ene-7, 7-ethylene dithiol (XXIV) as the product was obtained.

\[
\text{AcO} \quad \text{C}_{2}\text{H}_5\text{OC}_2\text{H}_5 \quad \rightarrow \quad \text{XXIV}
\]
Fieser reported that in several instances addition of BF$_3$-etherateto an acetic acid solution of 5α-cholestan-3, 6-dione (XXV) and Δ-cholestene-3,6-dione (XXVII) and excess of ethanedithiol at room temperature resulted in prompt separation of cholestan-3,6-dione bis-ethylenethioketal (XXVI) and Δ-cholestene-3,6-dione bis ethylenethioketal (XXVII-a).

\begin{align*}
\text{CH}_{17} & \quad \overset{\text{SH, AcOH}}{\underset{\text{BF}_3\text{-Et}_2\text{O}}{\text{r.t., 10 min.}}} \\
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\text{H} & \\
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\text{H} & \\
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\text{H} & \\
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\end{align*}

\begin{align*}
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\text{H} & \\
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\text{H} & \\
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\text{H} & \\
\text{C}_8 & \\
\text{H}_17 & \\
\text{O} & \\
\text{H} & \\
\end{align*}

Mushfiq and coworker reported the reactions of 3,6-dioxocholest-4-ene (XXVII), 3-oxocholest-4-ene (XXI), 3-oxo-6-bromocholest-4-ene (XXVIII) and 3-oxocholest-4,6-diene (XXIX) with 2-aminothiophenol and they obtained 6-oxo-5α-
cholestan [2'-α, 3'-b] benzothiazine (XXX), 6-oxo-5β-cholestan [2'-α, 3'-b] benzothiazine (XXXI), 3-spiro- Δ4-cholestbenzothiazine (XXXII), 3-spiro- Δ5-6-bromocholest benzothiazine (XXXIII) and (XXXIV) respectively as the products.
The reactions of 5α-cholestan-6-one (XXXV), 3β-acetoxy-5α-cholestan-6-one (XXXVI) and 3β-chloro-5α-cholestan-6-one (XXXVII)\(^{18a}\) with 2-mercaptoethanol in acetic acid, BF\(_3\) : Et\(_2\)O (as catalyst) at room temperature afforded (6S)-6,6-oxyethylene thio-5α-cholestane (XXXVIII), 3β-acetoxy-(6S)-6,6-oxyethylene thio-5α-cholestane (XXXIX), 3β-chloro-(6S)-6,6-oxyethylene thio-5α-cholestane (XL), (6R)-6,6-oxyethylene thio-5α-cholestane (XLI), 3β-acetoxy-(6R)-6,6-oxyethylene thio-5α-cholestane (XLII) and 3β-chloro-(6R)-6,6-oxyethylene thio-5α-cholestane (XLIII) as the products, respectively. Where as 3β,5-cyclo-5α-cholestan-6-one (XLIV) provided (XLV - XLVIII)\(^{18b}\).
(XLIV) $\xrightarrow{\text{C}_6\text{H}_6, \text{BF}_3: \text{Et}_2\text{O}}$ (XLV)

(XLVa) $-\text{SCH}_2\text{CH}_2\text{OH}$
(XLVb) $-\text{OCH}_2\text{CH}_2\text{SH}$
(XLVc) $-\text{SCH}_2\text{CH}_2\text{OAc}$

(XLVI) + (XLVII)

(XLVIIa) $-\text{OTS}$
(XLVIIb) $-\text{SCH}_2\text{CH}_2\text{OH}$
(XLVIIc) $-\text{SCH}_2\text{CH}_2\text{OAc}$
The reaction of 4,4-dimethylcholest-5-en-3-one (XLIX), cholest-5-en-3-one (L) and cholest-4-en-3-one (XXI) with β-mercaptopropanol in dry benzene afforded the corresponding isomeric oxathiolanes (LI, LII), (LIII, LIV) and (LV, LVI) respectively. 

\[ \text{HSCH}_2\text{CH}_2\text{OH} \quad \text{C}_6\text{H}_6 \]

\[ \text{XXI} \quad \text{LV} \quad \text{LVI} \]

The reaction of cholest-5-en-7-one (LVII), 3β-acetoxycholest-5-en-7-one (XXII) and 3β-chlorocholest-5-en-7-one (XXIII) and 3β-chlorocholest-5-en-7-one
(LVIII)$^{19a}$ with ethanedithiol gave cholest-5-ene-7,7-ethylene dithiol (LIX), 3β-acetoxycholest-5-ene-7,7-ethylenedithiol (XXIV) and 3β-chlorocholest-5-ene-7,7-ethylenedithiol (LX), respectively.

\[
\begin{array}{c}
\text{(LVII)} \quad \text{X} \\
\text{(XXIII)} \quad \text{OAc} \\
\text{(LVIII)} \quad \text{Cl}
\end{array} \quad \text{\rightarrow} \quad \begin{array}{c}
\text{(LIX)} \quad \text{X} \\
\text{(XXIV)} \quad \text{OAc} \\
\text{(LX)} \quad \text{Cl}
\end{array}
\]

Reaction of 3α,4α-epoxy-6-nitrocholest-5-ene (LXI) with urea in dimethylformamide gave isomeric steroidal oxazolidinones (LXII, LXIII)$^{19b}$ whereas the epoxide (LXI) with acrylonitrile in the presence of BF$_3$-etherate afforded (LXIV)$^{19c}$.

\[
\begin{array}{c}
\text{(LXI)} \quad \text{C}_8\text{H}_{17} \\
\text{H}^-\text{O}^-\text{H}^-\text{NO}_2 \\
\text{H}^-\text{N}^+\text{C}^-\text{NH}_2 \\
\text{H}^-\text{C}^-\text{N}^+\text{O}^+\text{CH}_3^2 \quad \text{(LXII)} \\
\text{H}^-\text{O}^-\text{N}^+\text{H}^-\text{NO}_2 \\
\text{H}^-\text{N}^+\text{O}^+\text{H}^-\text{NO}_2 \\
\text{H}^-\text{N}^+\text{O}^+\text{H}^-\text{NO}_2 \\
\text{H}^-\text{N}^+\text{O}^+\text{H}^-\text{NO}_2 \\
\text{(LXIII)}
\end{array}
\]
The reaction of cholest-5-ene (LXV\textsubscript{a}), 3\(\beta\)-chlorocholest-5-ene (LXV\textsubscript{b}) and 3\(\beta\)-acetoxycholest-5-ene (LXV\textsubscript{c}) with acetonitrile, bromine and sodium azide afforded 5-bromo-5\(\alpha\)-cholest-6\(\beta\)(1\') 5\' -methyltetrazole (LXVI\textsubscript{a}), 3\(\beta\)-chloro-5-bromo-5\(\alpha\)-cholest-6\(\beta\)-(1\') 5\' -methyltetrazole (LXVI\textsubscript{b}) and 5-bromo-5\(\alpha\)-cholest-3-en-6\(\beta\)(1\') 5\' -methyltetrazole (LXVI\textsubscript{c}) as the products\textsuperscript{20a}.
The reaction of 3β-chloro-5α-cholestan-6-one (XXXVII)\(^{20b}\) with excess of β-mercaptoacetic acid and ammonium carbonate in dry benzene afforded steroidal spirothiazolidinones (LXVII, LXVIII, LXIX) and 3α,5-cyclo-5α-cholestan-6-one (XLIV) as the products where as 5α-cholestane-3,6-dione (XXV) furnished (LXX-LXXI) as the products under identical conditions\(^{20c}\).
Pujari and coworkers\textsuperscript{20d,21,22} reported the reactions of cyclic five, six and seven membered ketones (LXXII, LXXV and LXXVIII) with thiocarbohydrazide and obtained tetrazinethiones (LXXIII, LXXVI and LXXIX). The products obtained were further refluxed with chloroacetic acid and sodium acetate resulting oxospirothiazolotetrazines (LXXIV, LXXVII and LXXX), respectively.
The reaction of hydroxy ketone (LXXXI) with benzoic hydrazide afforded $^{23}$ \[2,5,6\text{-triaryl}-4H-1,3,4\text{-oxadiazine} \] (LXXXII) as the product.
2-Acyl-5-chlorophenol (LXXXIII) gave the corresponding phenylhydrazone (LXXXIV) which on Fischer indole synthesis gave the respective 2-(p-chloro-O-hydroxyphenyl)-3-alkylindole (LXXXV)\textsuperscript{24}. 

\[ \text{HO} \quad \text{Ph-N-NH} \quad \text{HO} \quad \text{N-N-Ph} \]

\[ \text{Cl} \quad \text{R} \quad \text{Cl} \quad \text{R} \]

\[ R = \text{CH}_3, \text{C}_2\text{H}_5, \text{C}_3\text{H}_7 \]

(LXXXIII) \quad (LXXXIV) \quad (LXXXV)
Butler\textsuperscript{25} reported the reaction of open chain acetoin (LXXXVI) with urea and obtained (LXXXVII) as the product.

\[
\begin{array}{c}
\text{CH}_3\text{C-C-CH}_3 \\
\xrightarrow{H_2N-C-NH_2}\text{CH}_3\text{-N-N-H} \\
\end{array}
\]

(LXXXVI) \hspace{4cm} (LXXXVII)

Huke and coworkers\textsuperscript{26} carried out the reaction of chromones (LXXXVIII) and (LXXXIX) under aprotic basic conditions with chloroacetone and obtained (XC) and (XCI) as the products, respectively.

\[
\begin{array}{c}
\text{O} \\
\text{C}_3\text{H}_7 \hspace{1cm} \text{COMe} \\
\text{O} \\
\text{C}_3\text{H}_7 \hspace{1cm} \text{COMe} \\
\end{array}
\]

(LXXXVIII) \hspace{4cm} (XC) \hspace{4cm} (XCI)

Geoffrey et al.\textsuperscript{27} reported the reaction of 3-hydroxyflavon-4-one (XCII) and 3-hydroxy-2,3,4'-trimethoxyflavan-4-one (CXIII) with O-phenylenediamine and obtained (XCVI) and (XCV) as the products.
Pinhey and Rizzardo reported photochemical change of 3β-acetoxy-6-nitrocholest-5-ene (XCVI) in presence of sunlight and obtained 3β-acetoxy-6-nitrocholest-4-ene (XCVII), 3β-acetoxycholest-4,6-isoaxazole (XCVIII), 3β-acetoxycholest-4,6-oxazole (XCIX), 3β-acetoxycholest-4-en-6-one (C) and 6-nitrocholest-3,5-diene (CI) as the products.
The reaction of 2-bromo-2-nitrocamphane (CII) with sulfuric acid at -5° afforded anhydrobromonitrocamphane (CIII) whereas (CIV) gave (CV) as the product\textsuperscript{29}.

The reaction of hydroxyketone (CVI) with hydroxyl amine-hydrochloride\textsuperscript{30} furnished oxime (CVII) as the product which in presence of acetic anhydride gave isoxazoles (CIX).
Isoxazole (CXI) was obtained when hydroxyoxime (CX) was treated with pyridine under reflux condition. 31

\[
\begin{align*}
(CVI) & \quad \xrightarrow{\text{N\textsubscript{H}OH}} \quad (CVII) \\
& \quad \quad \xrightarrow{\text{Ac}_2\text{O}} \quad (CVIII) \\
& \quad \quad \quad \quad \downarrow \Delta \\
& \quad \quad \quad \quad \quad (CIX)
\end{align*}
\]
A number of papers dealing with the synthesis and biological activities of steroidal compounds having heterocyclic ring systems, containing spiro linkage have appeared\textsuperscript{1-11}. Motivated by the pharmacological importance of these compounds, an attempt has been made to synthesize steroidal spirotetrazine thiones (CXIV - CXVIII), from easily accessible steroidal ketones (XXXV, XXXVI, XXXVII, CXII and CXIII)\textsuperscript{32-34} in ethanol with thiocarbohydrazide\textsuperscript{35}. The thiones (CXIV-CXVIII) were also converted to corresponding oxospirothiazolotetrazines (CXIX - CXXIII) when treated with chloroacetic acid and sodium acetate in anhydrous ethanol under reflux conditions.

\[ R \]

\begin{align*}
(\text{XXXV}) & : H \\
(\text{XXXVI}) & : \text{OAc} \\
(\text{XXXVII}) & : \text{Cl} \\
(\text{CXII}) & : \text{Br} \\
(\text{CXIII}) & : \text{I}
\end{align*}
Reaction of 5α-cholestan-6-one (XXXV) with thiocarbohydrazide:

5α-Cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV):

5α-Cholestan-6-one (XXXV) was dissolved in ethanol and the reaction mixture was stirred for 15 minutes. To this mixture a solution of thiocarbohydrazide in acetic acid was added over a period of 15 minutes. After complete addition the reaction mixture was further stirred for 10 minutes. The progress of the reaction was monitored by TLC. The precipitated portion was filtered and taken up in ether. The ethereal solution was washed with water and sodium bicarbonate and dried over anhydrous sodium sulphate. The removal of the solvents gave an oily product which on crystallization from methanol furnished a compound m.p. 175°.

![XXXV](image)

![CXIV](image)
Characterization of the compound, m.p. 175° as 5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV):

The elemental analysis of the compound, m.p. 175° corresponded to the molecular formula C_{28}H_{50}N_{4}S. The IR spectrum of the compound exhibited bands at 3300 (N-H), 1650, 1510 (N-H), 1400 (C-N) and 1040 cm^{-1} (C=S). These values suggested the presence of tetrazinethione moiety, fused with steroid nucleus. The $^1$H-NMR spectrum of the compound displayed a multiplet centered at δ 6.0 (exchangeable with deuterium) and was assigned to (4X-NH). Methyl protons were observed at δ 1.2 (C10-CH$_3$), 0.72 (C13-CH$_3$), 0.91 and 0.81 (other methyl protons). On the basis of above evidences the compound, m.p. 175° was characterized as 5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV). The structure of the compound was further supported by its mass spectral studies. The mass spectrum of (CXIV) gave significant fragment ion peaks at m/z 386 (M$^+$-CH$_2$N$_3$S), 371, 252, 164 and 147. The tentative mechanism for the formation of these ions has been shown in Scheme-1.
Reaction of 5α-cholestane-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV) with chloroacetic acid and sodium acetate:

6'(7'H)-Oxospiro[5α-cholestan-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXIX):

5α-Cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV) was taken in anhydrous ethanol and to this solution chloroacetic acid, sodium acetate were added and the reaction mixture was refluxed for 5-6 hrs. After completion of the reaction, the reaction mixture was cooled and poured into ice cold water. Compound thus obtained was filtered, dried and
recrystallized from ethanol to provide crystalline solid, m.p. 139°.

Characterization of the compound, m.p. 139° as 6'(7'H)-oxo spiro[5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXIX):

The compound, m.p. 139° was analysed for C_{30}H_{50}N_{4}O_{5}. The IR spectrum of the compound exhibited bands at 3490-3200 (N-H), 1705 (C=O), 1630 (C=N) and 1480 cm\(^{-1}\) (C-N). The \(^1\)H-NMR spectrum of the compound exhibited a broad singlet at \(\delta\) 5.5 integrating for two protons and was assigned to (2X-N-H) (exchangeable with deuterium) and a singlet at \(\delta\) 2.2 for two protons (CH\(_2\)CO). Angular and side chain methyl protons were observed at \(\delta\) 1.2 (C10-CH\(_3\)), 0.75 (C13-CH\(_3\)), 0.90 and 0.80. These values suggested the compound to be 6'(7'H)-oxospiro [5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXIX).
This structure was further supported by mass spectral studies. The prominent fragment ion peaks were at m/z 440 (M^+ - C_2H_2OS) 401, 386, 327 and 312 in the mass spectrum of the compound (CXIX) and their formation was shown in Scheme-2.

**Scheme-2**

Reaction of 3β-acetoxy-5α-cholestan-6-one (XXXVI) with thiocarbohydrazide: 3β-Acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV):

3β-Acetoxy-5α-cholestan-6-one (XXXVI) was dissolved in ethanol and the reaction mixture was stirred for 15 minutes. To this mixture a solution of thiocarbohydrazide in acetic acid
was added under similar reaction conditions as described earlier. After usual work up and purification by crystallization a solid compound (CXV), m.p. 191° was obtained.

Characterization of the compound, m.p. 191° as 3β-acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV):

The compound, m.p. 191° was analysed correctly for C_{30}H_{52}O_{2}N_{4}S. The IR spectrum of the compound exhibited bands at 3250 (N-H), 1725 (CH_{3}COO-), 1630, 1510 (N-N), 1470 (C-N), 1240, 1030 (C=O) and 1020 cm^{-1} (C=S). These values suggested the presence of tetrazine thione moiety, fused with steroid nucleus. The ^1H-NMR spectrum of the compound displayed a multiplet centered at δ 6.4 (exchangeable with deuterium) and was assigned to (4X-N-H) and a multiplet centered at δ 4.7 integrating for one proton to C_{3α}-H (W_{2}/2 = 16Hz; axial). The acetate methyl protons were observed as singlet at δ 2.1 and the angular and side chain methyl protons were observed at
δ 1.2 (C10-CH₃), 0.75 (C13-CH₃), 0.91 and 0.81. These values suggested the compound to be 3β-acetoxy-5α-cholestan-6-spiro-1', 2',4',5'-tetrazine-3'-thione (CXV). This structure was further supported by mass spectral studies. The mass spectrum of the compound (CXV) gave prominent fragment ion peaks at m/z 444, 384, 369, 310 and lower mass ion peaks. Genesis of some of the prominent fragment ion peaks has been shown in Scheme-3.

Reaction of 3β-acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV) with chloroacetic acid and sodium acetate: 6'(7'H)-Oxospiro[3β-acetoxy-5α-cholestan]-6,3'(4'H)-[2H]thiazolo-[3,2-b]-s-tetrazine (CXX):

3β-Acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV) was taken in anhydrous ethanol and to this solution
chloroacetic acid, sodium acetate were added and the reaction mixture was refluxed for 5-6 hrs. After completion of the reaction, the reaction mixture was cooled and poured into ice cold water. Compound thus obtained was filtered, dried and recrystallized from ethanol to provide crystalline solid, m.p. 154°.

Characterization of the compound, m.p. 154° as 6'(7'H)-oxo-spiro[3β-acetoxy-5α-cholestan-6,3'(4'H)-]thiazolo[3,2-b]-s-tetrazine (CXX):

The compound, m.p. 154° was analysed correctly for C₃₂H₅₂N₄O₃S. The IR spectrum of the compound exhibited bands at 3500-3420 (N-H), 1740(CH₃CO-), 1710 (C=O), 1630 (C=N), 1490 (C-N) and 1040 cm⁻¹ (C-O). These values indicated the presence of oxospirothiazolotetrazine ring in the molecule. The ¹H-NMR spectrum of the compound displayed a broad singlet
at δ 4.8 integrating for two protons which was assigned to 
(2X-N-H) (exchangeable with deuterium) and a multiplet 
centered at δ 4.0 for C3α-H (W 1/2 = 18 Hz, axial) 36. The signals 
as singlets at δ 2.0 for -CH 2CO and at δ 1.9 for CH 3-COO were 
also obtained. Angular and side chain methyl protons were 
observed at δ 1.2 (C10-CH 3), 0.78 (C13-CH 3), and 0.91, and 
0.81. These values suggested the structure of the compound, 
m.p. 154° as 6′(7′H)-oxospiro[3β-acetoxy-5α-cholestan]-6,3′(4′H)-
[2H]thiazolo[3,2-b]-s-tetrazine (CXX). This structure was 
further supported by mass spectral data. The mass spectrum of 
the compound (CXX) gave prominent fragment ion peaks at m/z 512, 
438, 399, 384, 325 and 310. Scheme-4 explains the modes of 
their formation.
Reaction of 3β-chloro-5α-cholestan-6-one (XXXVII) with thiocarbohydrazide: 3β-Chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVI):

3β-Chloro-5α-cholestan-6-one (XXXVII) was dissolved in ethanol and the reaction mixture was stirred for 15 minutes. To this mixture a solution of thiocarbohydrazide in acetic acid was added under similar reaction conditions as described earlier. After usual work up and purification by crystallization a solid compound of m.p. 181° was obtained.

Characterization of the compound, m.p. 181° as 3β-chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVI):

The compound (CXVI) m.p. 181° was analysed correctly for C_{28}H_{49}N_{4}ClS (positive Beilstein test). The IR spectrum of the compound showed absorption bands at 3250 (N-H), 1640, 1530 (N-H), 1485 (C-N), 1010 (C=S) and 760 cm⁻¹ (C-Cl). These values indicated the presence of tetrazine thione moiety fused with
steroidal nucleus. The $^1$H-NMR spectrum of the compound displayed a multiplet centered at $\delta$ 5.6 integrating for (4X-N-H) (exchangeable with deuterium) and other multiplet centered at $\delta$ 3.8 for C3α-H ($\frac{\Delta}{2} = 16$ Hz). Angular and side chain methyl protons were observed at $\delta$ 1.2 (Cl0-CH$_3$), 0.70 (Cl3-CH$_3$), 0.91 and 0.80. These values suggested the structure of the compound, m.p. 181° as 3β-chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVI). This structure was further supported by mass spectral study of the compound. Prominent fragment ion peaks were obtained at m/z 420/422, 384, 369, 307/309, 286/288, 198/200, 162 and 147. Formation of these ions has been rationalized according to Scheme-5.

**SCHEME-5**

- m/z 420/422
- m/z 307/309
- m/z 384
- m/z 369
- m/z 162
- m/z 147
- m/z 286/288
- m/z 198/200
Reaction of 3β-chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVI) with chloroacetic acid and sodium acetate: 6'(7'H)-oxospiro[3β-chloro-5α-cholestan-1-6,3'(4'H)-[2H]thiazolo[3,2-b]-5-tetrazine (CXXI):

3β-Chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVI) was taken in anhydrous ethanol and to this solution chloroacetic acid and sodium acetate were added and the reaction mixture was refluxed for 5-6 hrs. After completion of the reaction and usual work up of the reaction mixture and recrystallization from ethanol provided a compound, m.p. 161°.

\[ \text{(CXVI)} \]

\[ \text{(CXXI)} \]

Characterization of the compound, m.p. 161° as 6'(7'H)-oxospiro [3β-chloro-5α-cholestan-1-6,3'(4'H)-[2H]thiazolo[3,2-b]-5-tetrazine (CXXI):

The compound (CXXI), m.p. 161° (positive Beilstein test)
was analysed for C_{30}H_{49}N_{4}ClO_{5}. The IR spectrum of the compound showed bands at 3480-3240 (N-H), 1710 (C=O), 1630 (C=N), 1470 (C-N) and 750 cm^{-1} (C-Cl). These values indicated the presence of oxospirothiazolotetrazine ring in the steroid nucleus.

The $^1$H-NMR spectrum of the compound displayed a broad singlet at $\delta$ 5.6 integrating for (2X-N-H) (exchangeable with deuterium) and other multiplet centered at $\delta$ 3.9 for C3α-H ($\frac{J}{2} = 16$ Hz). A singlet at $\delta$ 2.0 for two protons was assigned to -CH$_2$-CO. Angular and side chain methyl protons were observed at $\delta$ 1.2 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.90 and 0.80. In the light of above discussion the compound, m.p. 161° was characterized as 6'(7'H)-oxospiro[3β-chloro-5α-cholestan]-6,3'(4'H)-[2H]-thiazolo[3,2-b]-s-tetrazine (CXXI). This structure was further supported by mass spectral data. In the mass spectrum of the compound (CXXI) the prominent fragment ions were at m/z 512, 438, 399, 384, 325 and 310. The formation of these ions has been shown in Scheme-6.
Reaction of 3β-bromo-5α-cholestan-6-one (CXII) with thio-carbohydrazide: 3β-Bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVII):

3β-Bromo-5α-cholestan-6-one (CXII) was dissolved in ethanol and the reaction mixture was stirred for 15 minutes. To this mixture a solution of thio-carbohydrazide in acetic acid was added under similar reaction conditions as described earlier. Usual work up of the reaction mixture and purification by crystallization, a compound (CXVII) m.p. 148°, was obtained.

Characterization of the compound, m.p. 148° as 3β-bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXXVII):

The compound (CXVII) m.p. 148° was analysed correctly for C_{28}H_{49}N_{4}BrS (positive Beilstein test). The IR spectrum of the compound showed absorption bands at 3250 (N-H), 1640, 1510 (N-H), 1470 (C-N), 1040 (C=S) and 650 cm^{-1} (C-Br). These
values indicated the presence of tetrazine thione moiety fused with steroid nucleus. The $^1$H-NMR spectrum of the compound displayed a multiplet centered at δ 5.4 integrating for (4X-N-H) (exchangeable with deuterium) and other multiplet centered at δ 3.8 for C3α-H ($\frac{1}{2} = 16$Hz). Angular and side chain methyl protons were observed at δ 1.2 (C10-CH$_3$), 0.75 (C13-CH$_3$), 0.91 and 0.81. These values suggested the structure of the compound, m.p. 148° as 3β-bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVII). This structure was further supported by mass spectral data. Fragmentation pathway of some significant fragment ions such as m/z 464/466, 384, 369, 351/353, 330/332, 242/244, 162 and 147 has been shown in Scheme-7.
Reaction of 3β-bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVII) with chloroacetic acid and sodium acetate: 6'(7'H)-Oxospiro[3β-bromo-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXII):

3β-Bromo-6-spiro-1',2',4',5'-tetrazine-3'-thione (LXV) was taken in anhydrous ethanol and to this solution chloroacetic acid and sodium acetate were added and the reaction mixture was refluxed for 5-6 hrs. After completion of the reaction, the reaction mixture was worked up as usual and crystallization afforded the compound, m.p. 197°.

\[ \text{(CXVII)} \rightarrow \text{(CXXII)} \]

Characterization of the compound, m.p. 197° as 6'(7'H)-oxospiro[3β-bromo-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXII):

The compound, m.p. 197° (positive Beilstein test) showed elemental analysis compatible with molecular formula C_{30}H_{49}N_{4}BrOS. Its IR spectrum exhibited bands at 3420-3340 (N-H), 1725 (C=O),
1620 (C=N), 1480 (C-N) and 610 cm$^{-1}$ (C-Br). These values indicated the presence of oxospirothiazolotetrazine moiety in the steroid nucleus. The $^1$H-NMR spectrum of the compound displayed a broad singlet at $\delta$ 5.5(2X-N-H) (exchangeable with deuterium) and a multiplet centered at $\delta$ 3.8 for C3α-H ($\omega_{1/2}$ = 14 Hz) and two protons of (CH$_2$CO-) were observed at $\delta$ 2.1 as a singlet. Angular and side chain methyl protons were observed at $\delta$ 1.2 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.91 and 0.81. These values suggested the structure of the compound, m.p. 197°C as 6'(7'H)-oxospiro[3β-bromo-5α-cholestan:]6,3'(4'H)-[2H]-thiazolo[3,2-b]-s-tetrazine (CXXII). The fragment ion peaks in the mass spectrum of the compound (CXXII) were found at m/z 512, 438, 399, 384, 325 and 310. Genesis of these ions has been shown in Scheme-8.

**SCHEME - 8**

![Scheme 8 Diagram](image)
Reaction of 3β-iodo-5α-cholestan-6-one (CXIII) with thiocarbohydrazide: 3β-Iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII):

3β-Iodo-5α-cholestan-6-one (CXIII) was dissolved in ethanol and the reaction mixture was stirred for 15 minutes. To this mixture a solution of thiocarbohydrazide in acetic acid was added under similar reaction conditions as described earlier. Usual work up of reaction mixture and purification by crystallization furnished a pure solid compound, m.p. 156°.

Characterization of the compound, m.p. 156° as 3β-iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII):

The compound (CXVIII) m.p. 156° was analysed correctly for C_{28}H_{49}N_{4}S (positive Beilstein test). The IR spectrum of the compound showed absorption bands at 3240 (N-H), 1640, 1520 (N-H), 1480 (C-N), 1080 (C=S) and 800 cm^{-1} (C-I). These values
indicated the presence of tetrazine thione moiety\textsuperscript{20} fused with the steroid nucleus. The \textsuperscript{1}H-NMR spectrum of the compound displayed a multiplet centered at δ 5.3 integrating for (4X-N-H) (exchangeable with deuterium) and other multiplet centered at δ 3.7 for C3α-H (W\textsubscript{2} = 18 Hz)\textsuperscript{36}. Angular and side chain methyl protons were observed at δ 1.2 (Cl0-CH\textsubscript{3}), 0.75 (C13-CH\textsubscript{3}), 0.90 and 0.80. These values suggested the structure of the compound, m.p. 156° as 3β-iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII). The mass spectrum of (CXVIII) gave significant fragment ion peaks at m/z 512, 384, 378, 369, 290, 162 and 147. Formation of these ions was explained in Scheme-9.
Reaction of 3β-iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII) with chloroacetic acid and sodium acetate: 6'(7'H)-Oxospiro[3β-iodo-5α-cholestan-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXIII) :

3β-Iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII) was taken in anhydrous ethanol and to this solution chloroacetic acid, sodium acetate were added and the reaction mixture was refluxed for 5-6 hrs. After the completion of the reaction, the reaction mixture was cooled and poured into ice cold water, and worked up in usual manner followed by crystallization from ethanol to furnish a compound, m.p. 181°.

Characterization of the compound, m.p. 181° as 6'(7'H)-oxospiro [3β-iodo-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXIII) :

The compound, m.p. 181° (positive Beilstein test) was
analysed correctly for $C_{30}H_{49}N_{4}O$. Its IR spectrum exhibited bands at 3400-3240 (N-H), 1740 (C=O), 1640 (C=N), 1500 (C-N) and 800 cm$^{-1}$ (C-I). These values indicated the presence of oxospirothiazolotetrazine moiety$^{20}$ in the steroid nucleus. The $^1$H-NMR spectrum of the compound displayed a broad singlet at $\delta$ 5.6 integrating for two protons (2X-N-H) (exchangeable with deuterium) and a multiplet centered at $\delta$ 3.7 for C3α-H ($W_2^1 = 14$ Hz)$^{36}$. The two protons of (CH$_2$COO-) were observed at $\delta$ 2.0 as a singlet. Angular and side chain methyl protons were observed at $\delta$ 1.2 (C10-CH$_3$), 0.78 (C13-CH$_3$), 0.91 and 0.81. These values suggested the structure of the compound, m.p. 181$^\circ$ as 6'(7'H)-oxospiro[3β-iodo-5α-cholestan]-6,3'(4'H)-[2H]thiazolo-[3,2-b]-s-tetrazine (CXXIII). This structure was further supported by mass spectral data. Significant fragment ion peaks in the mass spectrum of (CXXIII) were obtained at m/z 512, 438, 399, 384, 325 and 310. Formation of these ions has been shown in Scheme-10.

**SCHEME-10**
Oxygen and nitrogen containing heterocyclic compounds were found to exhibit biological activities such as antibacterial\(^{37}\), antifungal\(^{38}\), antidepressant\(^{39}\), tuberculostatic\(^{40}\). Due to these medicinal importance we carried out the reaction of steroidal hydroxyketones with benzoic hydrazide and obtained steroidal oxazetenes with four membered oxygen and nitrogen containing heterocyclic ring fused with steroidal nucleus.

When \(3\beta,5\)-dihydroxy-5\(\alpha\)-cholestan-6-one (CXXIV), \(3\beta\)-acetoxy-5-hydroxy-5\(\alpha\)-cholestan-6-one (CXXV) and \(3\beta\)-chloro-5-hydroxy-5\(\alpha\)-cholestan-6-one (CXXVI) were treated with benzoic hydrazide in anhydrous ethanol and acetic acid afforded \(3\beta\)-hydroxy-5\(\alpha\)-cholestan-6-one[6,5-c]-oxazetene (CXXVII), \(3\beta\)-acetoxy-5\(\alpha\)-cholestan-6-one[6,5-c]-oxazetene (CXXVIII) and \(3\beta\)-chloro-5\(\alpha\)-cholestan-6-one[6,5-c]-oxazetene (CXXIX) as the products, respectively. The structure of these steroidal oxazetenes was established and supported by IR, \(^{1}\)H-NMR, mass and easy formation of their dreiding model.
Reaction of 3β,5-dihydroxy-5α-cholestan-6-one (CXXIV) with Benzoic hydrazide: 3β-Hydroxy-5α-cholestan(6,5-c)-oxazetene (CXXVII)

3β,5-Dihydroxy-5α-cholestan-6-one (CXXIV) in dry ethanol and glacial acetic acid was refluxed with benzoic hydrazide for 6 hrs. After completion of the reaction, the reaction mixture was poured into ice cold water and yellow solid thus obtained was filtered, and dried at room temperature and recrystallized from acetone to afford a compound, m.p. 138°.

\[
\begin{align*}
\text{C}_{18}H_{37} & \quad \text{O} \\
\text{HO} & \quad \text{HO} \\
\text{HO} & \quad \text{HO}
\end{align*}
\]

\[
\begin{align*}
\text{C}_{18}H_{37} & \quad \text{O} \\
\text{HO} & \quad \text{HO} \\
\text{HO} & \quad \text{HO}
\end{align*}
\]

(CXXIV) \quad \text{Refux}

(CXXVII)

Characterization of the compound, m.p. 138° as 3β-hydroxy-5α-cholestan(6,5-c)-oxazetene (CXXVII)

The compound (CXXVII) m.p. 138° was correctly analyzed for \(\text{C}_{27}\text{H}_{45}\text{NO}_2\). The presence of hydroxy group is revealed by IR band at 3400 cm\(^{-1}\). In its IR spectrum the other characteristic bands were at 1630 (C=N), 1020 (C=O) and 950 cm\(^{-1}\) (N-O). The \(\text{H}-\text{NMR}\) spectrum of the compound gave multiplet centered at \(\delta 3.6\) for
C₃α-H ($\omega_{\frac{1}{2}} = 18\text{Hz})^{36}$. The angular and side chain methyl protons were observed at $\delta$ 1.2 (C10-CH₃), 0.75 (C13-CH₃), 0.91 and 0.85 (other methyl protons). In the light of above discussion the compound, m.p. 138° may therefore be regarded as 3β-hydroxy-5α-cholestanol(6,5-c)-oxazetene. The structure of the compound (CXXVII) was further supported by mass spectral study. The mass spectrum of compound (CXXVII) gave molecular ion at 415 (C₂₇H₄₅NO₂) followed by other significant fragment ions at m/z 400, 397, 383, 381, 367, 302, 175 and 160 and other lower mass peaks. Genesis of some of the fragment ions are shown in Scheme-11.

**SCHEME-11**

![Scheme diagram](image)
Reaction of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (CXXV) with Benzoic hydrazide: 3β-Acetoxy-5α-cholestaño(6,5-c)-oxazetene (CXXVIII)

3β-Acetoxy-5-hydroxy-5α-cholestan-6-one (CXXV) in dry ethanol and glacial acetic acid was refluxed with benzoic hydrazide for 6 hrs. After completion of the reaction, the reaction mixture was poured into water and the solid obtained was filtered and dried at room temperature, and was recrystallized from acetone to give a compound (CXXVIII), m.p. 161°.

Characterization of the compound, m.p. 161° as 3β-acetoxy-5α-cholestan-6-one(6,5-c)-oxazetene (CXXVIII)

The compound (CXXVIII) m.p. 161° was analyzed for C29H47NO2. The IR spectrum of the compound gave bands at 1735 (CH₃COO−), 1610 (C=N), 1460, 1240 (C=O) and 1050 cm⁻¹ (N-O). In the ¹H-NMR spectrum of the compound (CXXVIII) a multiplet centered at δ 4.02 was observed for C3α−H (J₁/₂ = 18 Hz)³⁶. The acetate
methyl protons were observed at $\delta$ 2.0 as singlet ($\text{CH}_3\text{COO}^-$). Angular and side chain methyl protons were observed at $\delta$ 1.15 ($\text{ClO}-\text{CH}_3$), 0.75 ($\text{Cl3-CH}_3$), 0.95 and 0.85. In the light of above discussion the compound, m.p. 161$^\circ$ was characterized as 3$\beta$-acetoxyl-5$\alpha$-cholestanol(6,5-c)-oxazetene (CXXVIII). Further support for the structure of the compound was obtained by its mass spectral study. The compound (CXXVIII) showed molecular ion peak at $M^+$ 457 ($\text{C}_{29}\text{H}_{47}\text{NO}_3$) along with significant ion peaks at m/z 442, 397, 383, 381, 367, 344, 175 and 160 and lower mass peaks. Formation of some of the fragment ions has been shown in Scheme-12.
Reaction of 3β-chloro-5-hydroxy-5α-cholestan-6-one (CXXVI) with Benzoic hydrazide: 3β-Chloro-5α-cholestan(6,5-c)-oxazetene (CXXIX)

3β-Chloro-5-hydroxy-5α-cholestan-6-one (CXXVI) in dry ethanol and glacial acetic acid was refluxed with benzoic hydrazide under the similar reaction conditions as described in previous experiments. After completion of the reaction, the reaction mixture was poured into ice cold water, the solid thus obtained was filtered and air dried, and was recrystallized from acetone to give (CXXIX) m.p. 113°.

Characterization of the compound of m.p. 113° as 3β-chloro-5α-cholestan(6,5-c)-oxazetene (CXXIX)

The compound (CXXIX) m.p. 113° (positive Beilstein test) was correctly analyzed for $C_{27}H_{44}NOCl$. The IR spectrum of the compound gave bands at 1590 (C=N), 1010 (C-O), 920 (N-O), and 720 cm$^{-1}$ (C-Cl). The $^1$H-NMR spectrum of the compound gave a
multiplet centered at $\delta$ 3.4 for $C3\alpha-H$ ($W_2^1 = 16$ Hz)\textsuperscript{36}. Angular and side chain methyl protons were observed at $\delta$ 1.15 ($C10-CH_3$), 0.70 ($C13-CH_3$), 0.95 and 0.84. On the basis of above evidence the compound, m.p. 113° may therefore be characterized as $3\beta$-chloro-$5\alpha$-cholestanol(6,5-c)-oxazetene (CXXIX). Mass spectral study further supported the structure of the compound as (CXXIX). The mass spectrum of the compound (CXXIX) gave molecular ion peak at $M^+ 433/435 \left(C_{27}H_{44}NOCl\right)$ followed by other distinguishing peaks at $m/z$ 418/420, 383, 381, 367, 320/322, 175 and 160 and other lower mass peaks. Fragmentation pathway of important fragment ions has been rationalized according to Scheme-13.

**Scheme-13**

```
m/z 320/322 \rightarrow \begin{array}{c}C_8H_{17}^- \rightarrow \mathrm{CH}_3 \rightarrow m/z 418/420 \end{array}
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```
m/z 433/435 \left(C_{27}H_{44}NOCl\right)
```

```
m/z 381 \rightarrow [N] \rightarrow m/z 397 \rightarrow [NO]
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m/z 383 \rightarrow [O]
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m/z 160 \uparrow \rightarrow \mathrm{CH}_3
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m/z 175 \downarrow \rightarrow \mathrm{CH}_3
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m/z 367
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```
m/z 320/322 \rightarrow \begin{array}{c}C_8H_{17}^- \rightarrow \mathrm{CH}_3 \rightarrow m/z 418/420 \end{array}
```

```
m/z 433/435 \left(C_{27}H_{44}NOCl\right)
```

```
m/z 381 \rightarrow [N] \rightarrow m/z 397 \rightarrow [NO]
```

```
m/z 383 \rightarrow [O]
```

```
m/z 160 \uparrow \rightarrow \mathrm{CH}_3
```

```
m/z 175 \downarrow \rightarrow \mathrm{CH}_3
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m/z 367
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Experimental

All melting points were observed on a Kofler hot block and are uncorrected. IR spectra were obtained in KBr with a Perkin-Elmer 237 spectrophotometer. IR values are given in cm$^{-1}$. $^1$H-NMR spectra were run in CDCl$_3$ on a Varian A-60D instrument with Me$_4$Si as the internal standard and its values are given in ppm (δ) (s, singlet; br, broad and mc, multiplet centered at). The N-H signals disappeared on addition of D$_2$O with no significant change in other part of spectra. Mass spectra were measured on JMS-300 spectrometer. The values of fragment ions from various compounds are given, the values in parentheses are the relative abundance (%) of the peaks with respect to the base peak as 100%. Thin layer chromatographic (TLC) plates were coated with silica gel and sprayed with 20% aqueous solution of perchloric acid. Silica gel (~20 g) was used for each gram of the material to be separated in column chromatography. Petroleum ether refers to a fraction of b.p. 40-60°C.

3β-Tosyloxycholest-5-ene

Cholesterol (50 g) was dissolved in pyridine (100 ml, freshly distilled over KOH) and p-toluene sulphonyl chloride (50 g) was added. A white crystalline precipitate was obtained within 5 minutes. After this, reaction mixture was kept over night at room temperature. The product was filtered and taken up in ether. The ethereal layer was washed with water, sodium
bicarbonate solution (5%) and again with water, dried over anhy-
drous sodium sulphate. Ether was evaporated over water bath and
the oil obtained was crystallized from petroleum ether to give
tosylate (3 g), m.p. 130° (reported \(40^a\), m.p. 131.5–132.5°).

**3β-Tosyloxy-6-nitrocholest-5-ene**

3β-Tosyloxycholest-5-ene (10 g) was treated with nitric acid (250 ml, d, 1.52) and sodium nitrite (10 g) was gradually added over a period of 1 hr with continuous stirring. Slight cooling was required during the course of reaction. Stirring was continued for additional 2 hrs. A yellow spongy mass was separated out on the surface of the mixture. The reaction mixture was diluted with cold water (250 ml). A green coloured solution was obtained. The whole mass was extracted with ether and it was washed successively with water, sodium bicarbonate solution (4%) and again with water. The ethereal solution was then dried over anhydrous sodium sulphate and filtered. Removal of the solvent provided an oil which was recrystallized from methanol to yield 3β-tosyloxy-6-nitrocholest-5-ene (6.8 g), m.p. 162° (reported \(40^a\), m.p. 162°).

**3β-Chlorocholest-5-ene**

Freshly purified thionyl chloride (75 ml) was added gradually to cholesterol (100 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 1 hr and then poured on to crushed ice water mixture with stirring. The yellow solid thus obtained was filtered under suction and washed several times with ice cooled water and air dried. Recrystallization of crude product from acetone gave 3β-chlorocholest-5-ene (95.5 g), m.p. 95-96° (reported41 96-97°). It gave positive Beilstein test and a yellow colour with tetranitromethane in chloroform.

**Cholest-5-ene**

3β-Chlorocholest-5-ene (15.0 g) was dissolved in warm amyl alcohol (300 ml) and sodium metal (35.0 g) was added in small portions to the solution with continuous stirring over a period of 8 hrs. The reaction mixture was heated now and then 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 over night. A white crystalline solid was obtained which was filtered under suction and washed thoroughly with water and air dried. Recrystallization of the crude material from acetone gave the desired compound in cubes (10.8 g), m.p. 93° (reported43, m.p. 89.5-91.2°).

**6-Nitrocholest-5-ene**

A suspension of freshly powdered cholest-5-ene (6.0 g) in glacial acetic acid (50 ml) was stirred at room
temperature for 5 minutes. Fuming nitric acid (20 ml, d, 1.5) was rapidly added and the stirring was continued for 2 hrs. The temperature of the reaction mixture was controlled between 20-25° by external cooling. The reaction mixture was then poured into ice cold water. A yellow solid thus obtained was filtered under suction, washed thoroughly with water and air dried. Recrystallization from ethanol furnished pure 6-nitrocholest-5-ene (3.5 g), m.p. 117-118° (reported m.p. 117-118°).

5α-Cholestan-6-one (XXXV)

6-Nitrocholest-5-ene (6 g) was powdered, dissolved in warm glacial acetic acid (120 ml) and zinc dust (12 g) was gradually added with shaking. The suspension was heated under reflux for 4 hrs and water (12 ml) was added now and then during the course of reaction. The hot solution was filtered to remove zinc powder, cooled to room temperature and diluted with a large excess of ice-cold water. The precipitate thus obtained was taken in ether and the ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Removal of the solvent gave the ketone (XXXV) as an oil which was crystallized from ethanol as thin plates (3.5 g), m.p. 96-98° (reported m.p. 98-100°).
**3β-Acetoxycholest-5-ene**

A mixture of cholesterol (50 g), pyridine (75 ml, freshly distilled over KOH) and freshly distilled acetic anhydride (50 ml) was heated on water bath for 2 hrs. The resulting brown solution was poured into 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 pure 3β-acetoxycholest-5-ene (45.0 g), m.p. 112° (reported m.p. 113°).

**3β-Acetoxy-6-nitrocholest-5-ene**

3β-Acetoxycholest-5-ene (10.0 g) was covered with nitric acid (250 ml; d, 1.42) and sodium nitrite (8.0 g) was gradually added over a period of 1 hr with continuous stirring. Slight cooling was also affected during the course of reaction and stirring was continued for additional 2 hrs. When the yellow spongy mass separated on the surface of the mixture, it was diluted with cold water (200 ml) resulting a green coloured solution. The whole mass was extracted with ether. The ethereal solution was washed with water, sodium bicarbonate solution (5%) (until washing was pink) and water and dried over sodium sulphate (anhydrous). Removal of the solvent provided the nitro compound as an oil which was crystallized from methanol (7.0 g), m.p. 104° (reported m.p. 102-104°).
3β-Acetoxy-5α-cholestan-6-one (XXXVI)

3β-Acetoxy-6-nitrocholest-5-ene (3 g) was powdered and dissolved in glacial acetic acid (125 ml) by warming the mixture and zinc dust (6 g) was added in small portions with shaking. The suspension was heated under reflux for 4 hrs and water (6 ml) was added now and then during the course of reaction. The hot solution was filtered to remove zinc, cooled to room temperature and diluted with a large excess of ice-cold water. The white precipitate thus obtained was taken in ether and the ethereal solution was washed successively with water sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was recrystallized from methanol to give (XXXVI) (2.4 g), m.p. 128° (reported m.p. 127-128°).

3β-Chloro-6-nitrocholest-5-ene

To a well stirred mixture of 3β-chlorocholest-5-ene (12 g) glacial acetic acid (80 ml) and nitric acid (25 ml, d, 1.52) at temperature below 20°, was added sodium nitrite (3.0 g) gradually over a period of 3 hrs. After the complete addition of sodium nitrite, the mixture was further stirred for about 1 hr, ice cooled water (200 ml) was added and the yellowish solid thus separated was filtered and air dried. The desired nitro compound was recrystallized from methanol as needles (8.3 g), m.p. 151-152° (reported m.p. 153°).
3β-Chloro-5α-cholestan-6-one (XXXVII)

To a solution of 3β-chloro-6-nitrocholest-5-ene (12 g) in hot distilled glacial acetic acid (240 ml), zinc dust (24 g) was added gradually in small portions with shaking. The suspension was heated under reflux for 4 hrs and water (24 ml) was added at regular intervals during the course of the reaction. The hot solution was filtered to remove zinc and the filtrate was cooled to room temperature and diluted with a large excess of ice cold water. The organic matter was extracted with ether, the ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was crystallized from methanol to give the ketone (XXXVII) (8.7 g) m.p. 128-129° (reported33 m.p. 128-129°).

3α,5-Cyclo-5α-cholestan-6-one

3β-Chloro-5α-cholestan-6-one (XXXVII) (2.5 g) was dissolved in methanolic potassium hydroxide (50 ml, 5%) and the contents were refluxed for 1 hr. The progress of the reaction was monitored by TLC and after completion of the reaction, the reaction mixture was poured into ice cold water, solid thus obtained was filtered, washed with water, air dried and was recrystallized from methanol to afford the desired cycloketone, (1.75 g), m.p. 96° (reported34, m.p. 96-98°).
3β-Bromo-5α-cholestan-6-one (CXII)

3α,5-Cyclo-5α-cholestan-6-one (1.5 g) was heated under reflux for 8 hrs with 1.25 ml of HBr (48%) in acetone (37.0 ml). The solvent was removed under reduced pressure and the residue was diluted with 10 ml of water and the contents were taken in ether. The ethereal layer was washed with water, sodium bicarbonate solution (5%) and again with water and was dried over anhydrous sodium sulphate. Evaporation of the solvent provided an oil which was recrystallized from methanol to give 3β-bromo-5α-cholestan-6-one (CXII), (0.8 g), m.p. 126° (reported m.p. 126-127°).

3β-Iodo-5α-cholestan-6-one (CXIII)

3α,5-Cyclo-5α-cholestan-6-one (1.7 g) was dissolved in glacial acetic acid (25.0 ml) and treated with hydroiodic acid (5 ml, 54%). The turbid solution was made clear by the addition of ether. The mixture was kept at room temperature over night and then it was poured into ice cold water, extracted with ether. The ethereal extract was washed with water, sodium bicarbonate solution (5%) and finally with water. Removal of the solvent gave an oil which on crystallization from methanol gave 3β-iodo-5α-cholestan-6-one (CXIII), (1.27 g), m.p. 138° (reported m.p. 138-139°).
Reaction of 5α-cholestan-6-one (XXXV) with thiocarbohydrazide:

5α-Cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV)

5α-Cholestan-6-one (XXXV) (1 g, 2.60 m mol) was dissolved in ethanol (15 ml) and the mixture was stirred for 15 minutes. To this mixture a solution of thiocarbohydrazide (1 g, 9.40 m mol) in acetic acid (20 ml) was added over a period of 15 minutes. After complete addition of thiocarbohydrazide solution, the reaction mixture was further stirred for 10 minutes. The progress of the reaction was monitored by TLC. The precipitate obtained was filtered and taken in ether. The ethereal solution was washed with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent provided an oily residue which on crystallization from methanol furnished 5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV) (0.80 g, 1.70 m mol) m.p. 175°.

Analysis Found : C, 70.8; H, 10.4; N, 11.8
C28H50N4S requires : C, 70.9; H, 10.5; N, 11.8%

IR : $\nu_{\text{max}}$ 3300 (N-H), 1650, 1510 (N-H), 1400 (C-N) and 1040 cm$^{-1}$ (C=S).

$^1$H-NMR : $\delta$ 6.0 (mc, 4H-N-H), 1.2 (C10-CH$_3$), 0.72 (C13-CH$_3$), 0.91 and 0.81 (other methyl protons).

MS : 474 (C$_{28}$H$_{50}$N$_4$S, M$^+$ absent)m/z 386 (6.42, C$_{27}$H$_{48}$N), 385 (17.49), 384 (100.00), 371 (1.8; C$_{26}$H$_{43}$N), 370 (4.06), 369 (31.7), 368 (4.06), 367 (6.42), 366 (26.5), 356 (8.92), 355 (4.09), 354 (2.09), 271 (6.02), 252 (2.03; C$_{12}$H$_{20}$N$_4$S),
Reaction of 5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV) with chloroacetic acid and sodium acetate: 6'-(7'H)-Oxo-spiro[5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-5-tetrazine (CXIX)

5α-Cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXIV) (2 g, 3.89 m mol), chloroacetic acid (1 g) and fused sodium acetate (0.9 g) were taken in anhydrous ethanol (50 ml) and the mixture was heated under reflux for 5 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was concentrated, cooled and kept overnight
The solid thus obtained was filtered washed well with water and dried. The recrystallization of the solid compound from ethanol gave 6'(7'H)-oxospiro[5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CIXIX) (1.20 g, 2.35 m mol) m.p. 139°.

Analysis Found : C, 70.0; H, 9.6; N, 10.8
C₃₀H₅₀N₄OS requires : C, 70.0; H, 9.7; N, 10.8%

IR : \text{max. } 3490-3200 \text{ (N-H), } 1705 \text{ (C=O), } 1630 \text{ (C=N), and } 1480 \text{ cm}^{-1} \text{ (C-N).}

^1H-NMR : \delta 5.5 \text{ (brs, 2X-N-H), } 2.2 \text{ (s, 2H, CH}_{2}CO^{-}), \text{ 1.2 (C10-CH}_{3}), 0.75 \text{ (C13-CH}_{3}), \text{ 0.90 and 0.80 (other methyl protons).}

MS : 514 \text{ (C}_{30}H_{50}N_{4}OS, M^{+} \text{ absent), } 440 \text{ (4.29; C}_{28}H_{48}N_{4}), 439 \text{ (1.43), } 430 \text{ (2.15), } 428 \text{ (1.43), } 417 \text{ (14.30), } 416 \text{ (67.21), } 415 \text{ (81.51), } 414 \text{ (8.58), } 413 \text{ (4.29), } 412 \text{ (2.86), } 411 \text{ (1.43), } 410 \text{ (0.72), } 406 \text{ (0.72), } 405 \text{ (5.72), } 404 \text{ (18.59), } 403 \text{ (60.06), } 402 \text{ (81.51), } 401 \text{ (0.72), } 400 \text{ (4.29), } 399 \text{ (2.15), } 396 \text{ (4.29), } 395 \text{ (1.43), } 393 \text{ (4.29), } 392 \text{ (5.72), } 391 \text{ (28.60), } 390 \text{ (4.29), } 389 \text{ (7.15), } 388 \text{ (14.30), } 387 \text{ (12.87), } 386 \text{ (1.43), } 384 \text{ (7.15), } 383 \text{ (18.59), } 382 \text{ (42.90), } 381 \text{ (12.44), } 380 \text{ (4.29), } 373 \text{ (2.15), } 372 \text{ (4.29), } 371 \text{ (12.44), } 370 \text{ (14.30), } 369 \text{ (12.87), } 368(35.75), 367 \text{ (81.51), } 366 \text{ (100.00), } 365 \text{ (48.62), } 364 \text{ (10.01), } 363 \text{ (0.72), } 359 \text{ (2.15), } 358 \text{ (5.72), } 357 \text{ (17.16), } 356 \text{ (10.44), } 355(53.91), 353 \text{ (17.16), } 352 \text{ (20.02), } 351 \text{ (2.86), } 345(4.29),
344 (8.58), 343 (21.45), 342 (10.01), 341 (18.59), 340 (54.87),
339 (18.59), 338 (1.43), 328 (6.65), 327 (18.59), 326 (6.65),
325 (4.29), 314 (5.72), 313 (21.45), 312 (2.86), 310 (10.01),
300 (4.29), 299 (4.29), 298 (6.65), 275 (5.72), 274 (11.44),
270 (1.43), 264 (4.29), 263 (5.72), 262 (5.72), 261 (21.45),
260 (10.01), 259 (11.44), 258 (24.31), 257 (5.72), 251 (8.58),
250 (4.29), 245 (21.45), 244 (20.02), 243 (20.02), 240 (6.65),
237 (45.76), 236 (4.29), 230 (30.03), 229 (15.73), 226 (8.58),
214 (30.03), 213 (11.44), 210 (5.72), 204 (20.02), 203 (10.01),
202 (10.01), 201 (38.61), 200 (30.03), 199 (14.30), 198 (11.44),
190 (24.31), 189 (45.76), 188 (21.45), 187 (20.02), 186 (20.02),
177 (18.59), 176 (38.61), 175 (34.32), 174 (32.89), 173 (22.88),
171 (22.88), 170 (8.58), 161 (97.54), 160 (85.80), 159 (60.06),
158 (42.90), 157 (21.45), 156 (21.45), 150 (14.30), 148 (42.90),
147 (95.71), 146 (45.76), 145 (30.03), 144 (35.34), 143 (21.45),
142 (21.45), 131 (60.06), 128 (42.90), 121 (24.31), 120 (11.44),
119 (30.03), 117 (35.75), 110 (7.15), 109 (34.32), 108 (14.30),
107 (72.93), 106 (15.73), 105 (60.06), 104 (7.15), 103 (10.01),
98 (71.50), 96 (57.20), 94 (10.01), 93 (72.93), 80 (98.57), 78
(60.06), 76 (28.60), 70 (36.18), 68 (60.06), 66 (53.20), 57
(5.72), 56 (72.93), 55 (20.02), 54 (98.57), 53 (5.72), 50 (4.29),
49 (2.86), 48 (1.42), 45 (30.03), 44 (31.46), 43 (98.57), 42
(98.57), 41 (31.46), 40 (25.74).
Reaction of 3β-acetoxy-5α-cholestan-6-one (XXXVI) with thiocarbohydrazide: 3β-Acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV)

3β-Acetoxy-5α-cholestan-6-one (CXV) (1 g, 2.25 m mol) was dissolved in ethanol (15 ml) and a solution of thiocarbohydrazide (1 g, 9.40 m mol) in acetic acid (20 ml) was added over a period of 15 minutes under the similar reaction conditions as described earlier. Usual work up of the reaction mixture and evaporation of the solvent gave an oily residue which on recrystallization from methanol furnished 3β-acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV) (0.80 g, 1.5 m mol) m.p. 191°C.

Analysis Found : C, 67.5; H, 9.7; N, 10.5
C_{30}H_{52}O_{2}N_{4}S requires : C, 67.7; H, 9.8; N, 10.5%.

IR : ν_{max} 3250 (N-H), 1725 (CH_{3}COO-), 1630, 1510 (N-H), 1470 (C-N), 1240, 1030 (C-O) and 1020 cm^{-1} (C=S).

$^{1}$H-NMR : δ 6.4 (mc, 4X-N-H), 4.7 (mc, C3α-H; W_{2}/2 = 16 Hz, axial) 2.1 (s, CH_{3}COO-), 1.2 (C10-CH_{3}), 0.75 (C13-CH_{3}), 0.91 and 0.81 (other methyl protons).

MS : M^{+} 532 (C_{30}H_{52}O_{2}N_{4}S, absent), m/z 444 (26.2, C_{29}H_{50}O_{2}N), 399 (12.3), 385 (32.4), 384(5.60), 382(100.00; C_{27}H_{46}N), 369 (21.6,C_{26}H_{43}N), 325 (12.3), 310 (4.0), 108 (6.42), 107 (6.42), 106 (99.7), 91 (4.0), 89 (4.6), 76 (4.2), 75 (21.6), 74 (12.3), 62 (4.0), 60(50.6), 59 (32.4), 58 (4.65), 57 (4.62), 48 (13.30), 44 (6.42), 43 (30.3), 42 (11.63), 41 (6.42).
Reaction of 3β-acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV) with chloroacetic acid and sodium acetate: 6'(7'H)-Oxospiro[3β-acetoxy-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXX)

3β-Acetoxy-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXV), (2 g, 3.50 m mol), chloroacetic acid (1 g) and fused sodium acetate (0.9 g) were taken in anhydrous ethanol (50 ml) and the mixture was heated under reflux for 5 hrs. Usual workup of the reaction mixture as described earlier gave a solid, which was recrystallized from ethanol to give 6'(7'H)-oxo-spiro[3β-acetoxy-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXX) (1.30 g, 2.27 m mol) m.p. 154°.

Analysis Found : C, 67.1; H, 9.1; N, 9.7

C\textsubscript{32}H\textsubscript{52}N\textsubscript{4}O\textsubscript{3}S requires : C, 67.1; H, 9.1; N, 9.8%.

IR : \(\nu\)max. 3500-3420 (N-H), 1740 (CH\textsubscript{3}CO-), 1710 (C=O), 1630 (C=N), 1490 (C-N) and 1040 cm\textsuperscript{-1} (C-O).

\textsuperscript{1}H-NMR : \(\delta\) 4.8 (brs, 2X-N-H), 4.0 (mc, C3α-H; \(\text{J}_{2} = 18\) Hz, axial), 2.0 (s, 2H, CH\textsubscript{2}CO), 1.9 (s, 3H, CH\textsubscript{3}COO), 1.2 (C10-CH\textsubscript{3}), 0.78 (C13-CH\textsubscript{3}), 0.91 and 0.81 (other methyl protons).

MS : 572 (C\textsubscript{32}H\textsubscript{52}N\textsubscript{4}O\textsubscript{3}S , absent), 512 (12.60), 459 (2.80), 438(2.80; C\textsubscript{28}H\textsubscript{46}N\textsubscript{4}), 437 (1.40), 430 (4.20), 421 (2.80), 410 (1.40), 409 (5.60), 408 (2.80), 400 (11.20), 399 (71.40), 398 (61.60), 397 (4.20), 396 (2.80), 395 (1.40), 394 (1.40), 384 (5.60), 382 (5.60), 381 (22.40), 380 (85.40), 379
Reaction of 3β-chloro-5α-cholestan-6-one (CXXXIV) with thiocarbohydrazide

3β-Chloro-5α-cholestan-6-one (CXXXIV) (1 g, 2.48 m mol) was
dissolved in ethanol (15 ml). To this mixture a solution of thiocarbohydrazide (1 g, 9.40 m mol) in acetic acid (20 ml) was added over a period of 15 minutes under the similar reaction conditions as described earlier. Usual workup and recrystallization from methanol furnished 3β-chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVI) (0.70 g, 1.38 m mol) m.p. 181°.

Analysis Found : C, 66.0; H, 9.5; N, 11.0

C_{28}H_{49}N_{4}ClS requires : C, 66.1; H, 9.6; N, 11.0%

IR : \( \nu_{\text{max}} \) 3250 (N-H), 1640, 1530 (N-H), 1485 (C-N)
1010 (C=S) and 760 cm\(^{-1} \) (C-Cl).

\(^1\)H-NMR : \( \delta \) 5.6 (mc, 4X-N-H), 3.8 (mc, C3α-H; W\( ^1/2 \) = 16 Hz, axial), 1.2 (Cl10-CH\(_3\)), 0.70 (Cl13-CH\(_3\)), 0.91 and 0.80 (other methyl protons).

MS : M\(^+\) 508/510 (C\(_{28}\)H\(_{46}\)N\(_4\)ClS; Absent), m/z 420/422 (41.80/14.02; C\(_{27}\)H\(_{47}\)NCl), 421 (15.01), 419 (0.42), 409 (1.08), 407 (1.08), 405 (1.68), 404 (0.21), 403 (0.21), 402 (0.42), 401 (0.21), 387 (0.42), 386 (1.26), 385 (2.10), 384 (15.55; C\(_{27}\)H\(_{46}\)N\(_2\)), 383 (0.21), 382 (0.20), 370 (0.16), 369 (0.5; C\(_{26}\)H\(_{43}\)N), 368 (1.68), 367 (1.68), 366 (0.15), 365 (0.42), 355 (0.12), 353 (0.21), 335 (0.16), 331 (0.29), 320 (0.21), 310 (0.42), 309 (9.10), 308 (1.68), 307 (30.46), 306 (0.15), 305 (0.14), 286/288 (0.54/0.18; C\(_{12}\)H\(_{19}\)N\(_4\)Cl), 198/200 (0.48/0.16; C\(_{11}\)H\(_{17}\)NCl), 197 (0.42), 196 (0.21), 195 (0.32), 193 (0.21),
191 (0.16), 190 (0.12), 188 (0.32), 187 (0.22), 185 (0.21),
183 (0.21), 181 (0.20), 179 (0.13), 178 (0.12), 176 (0.19), 172
(0.12), 171 (0.12), 165 (0.21), 164 (0.29), 163 (0.42), 162
(0.21; C_{11}H_{16}N), 161 (1.68), 160 (0.21), 159 (3.78), 158 (0.21),
157 (3.36), 156 (0.21), 155 (0.20), 153 (0.21), 152 (0.42), 151
(0.29), 150 (1.26), 149 (24.8), 148 (1.36), 147 (1.54; C_{10}H_{13}N),
146 (0.21), 145 (0.84), 144 (0.21), 143 (1.26), 142 (0.42), 141
(0.21), 140 (0.15), 139 (0.14), 138 (0.21), 137 (1.68), 136
(30.26), 135 (2.10), 134 (1.68), 133 (1.26), 132 (1.26), 130
(0.20), 125 (0.14), 124 (0.42), 123 (2.56), 122 (2.10), 121
(1.16), 120 (0.84), 119 (1.68), 118 (0.16), 117 (1.20), 116
(0.21), 115 (0.89), 112 (0.19), 111 (0.39), 106 (0.05), 75
(30.6), 74 (8.4), 72 (0.84), 71 (0.21), 69 (0.20), 68 (0.20),
67 (0.85), 66 (0.21), 62 (0.15), 61 (0.21), 60 (30.3), 59 (28.28),
58 (0.21), 57 (0.42), 56 (0.21), 55 (0.13), 48 (1.26), 47 (0.29),
46 (0.12), 45 (9.76), 44 (1.26), 43 (0.23), 42 (100.00), 41
(4.25), 40 (0.21).

Reaction of 3β-chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-
3'-thione (CXVI) with chloroacetic acid and sodium acetate:
6'(7'H)-Oxospiro[3β-chloro-5α-cholestan]-6,3'(4'H)-[2H]thiazolo
[3,2-b]-5-tetrazine (CXXI)

3β-Chloro-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-
thione (CXVI), (2 g, 3.93 mmol), chloroacetic acid (1 g) and
fused sodium acetate (0.9 g) were taken in anhydrous ethanol
(50 ml) and the mixture was heated under reflux for 5 hrs. Usual workup of the mixture as described earlier gave a solid which was recrystallized from ethanol to furnish 6'(7'H)-oxospiro[3β-chloro-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXI) (1.15 g, 2.10 m mol) m.p. 161°.

Analysis Found : C, 65.7; H, 8.8; N, 10.2
C_{30}H_{49}N_4ClOS requires : C, 65.7; H, 8.9; N, 10.2%

IR : \( \gamma \) max. 3480-3240 (N-H), 1710 (C=O), 1630 (C=N)
1470 (C-N) and 750 cm\(^{-1}\) (C-Cl).

\(^1\)H-NMR : \( \delta \) 5.6 (brs, 2X-N-H), 3.9 (mc, C3α-H; \( \omega \) = 16 Hz, axial),
2.0 (s, CH$_2$COO), 1.2 (ClO-CH$_3$), 0.70 (Cl3-CH$_3$), 0.90,
and 0.80 (other methyl protons).

MS : 548/550 (C$_{30}$H$_{49}$N$_4$ClOS, absent), 512 (11.60), 438 (1.45;
C$_{28}$H$_{46}$N$_4$), 436 (4.35), 435 (2.90), 428 (2.90), 427 (1.45),
424 (5.80), 422 (10.15), 421 (8.70), 420 (33.35), 418 (5.80),
409 (2.90), 406 (4.35), 405 (7.25), 404(5.80), 399 (5.80),
398 (14.50), 397 (7.25), 386 (7.25), 385 (33.35), 384
(100.00), 383 (10.15), 382 (7.25), 381 (2.90), 380 (2.90),
370 (15.95), 369 (65.25), 368 (87.00), 367 (11.60), 356
(5.80), 355 (23.20), 354 (23.20), 353 (13.05), 352 (24.65),
351 (2.90), 350 (1.45), 325 (5.80), 310 (10.15), 307 (14.50),
288 (4.35), 279 (8.70), 271 (11.60), 267 (11.60), 266 (13.05),
265 (24.65), 264 (5.80), 261 (10.15), 260 (26.10), 259 (7.25),
255 (21.75), 247 (36.25), 246 (7.25), 245 (7.25), 244 (5.80),
243 (7.25), 230 (7.25), 229 (17.40), 228 (5.80), 215 (10.15),
Reaction of 3β-bromo-5α-cholestane-6-one (CXII) with thiocarbohydrazide: 3β-Bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVII)

3β-Bromo-5α-cholestan-6-one (CXII) (1 g, 2.23 m mol) was dissolved in ethanol (15 ml). To this mixture a solution of thiocarbohydrazide (1 g, 9.40 m mol) in acetic acid (20 ml) was added over a period of 15 minutes under the similar reaction conditions as described earlier. Usual workup and recrystallization of the semi-solid obtained from ethanol furnished 3β-bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVII) (0.70 g, 1.27 m mol) m.p. 148°.
Analysis Found: C, 60.4; H, 8.6; N, 9.8

C\textsubscript{28}H\textsubscript{49}N\textsubscript{4}BrS requires: C, 60.8; H, 8.9; N, 10.1%.

IR: $\nu_{\text{max}}$ 3250 (N-H), 1640, 1510 (N-H), 1470 (C-N), 1040 (C=S) and 650 cm\(^{-1}\) (C-Br).

\(^1\)H-NMR: $\delta$ 5.4 (mc, 4\textit{X}-N-H), 3.8 (mc, C3\textalpha{}-H; $J_{1/2} = 16$ Hz, axial), 1.2 (ClO-CH\textsubscript{3}), 0.75 (Cl3-CH\textsubscript{3}), 0.91 and 0.81 (other methyl protons).

MS: 552/554 (C\textsubscript{28}H\textsubscript{49}N\textsubscript{4}BrS, absent) 464/466 (7.2/7.5; C\textsubscript{27}H\textsubscript{47}NBr), 466 (25.0), 464 (27.5), 463 (80.0), 452 (2.5), 451 (7.5), 450 (5.0), 449 (2.5), 448 (2.5), 389 (1.25), 388 (2.5), 387 (12.5), 386 (30.0), 385 (17.5), 384 (15.0; C\textsubscript{27}H\textsubscript{46}N), 383 (2.5), 382 (2.5), 381 (1.25), 380 (1.25), 379 (2.5), 378 (0.62), 372 (2.5), 371 (7.5), 370 (5.0), 369 (17.5; C\textsubscript{26}H\textsubscript{43}N), 368 (2.5), 367 (5.0), 366 (3.75), 357 (0.62), 356 (5.0), 355 (5.00), 354 (7.5), 353 (25.0), 352 (8.75), 351 (24.75), 350 (2.5), 349 (12.5), 339 (1.25), 337 (0.42), 335 (1.25), 330/332 (5.0/4.75; C\textsubscript{12}H\textsubscript{19}N\textsubscript{4}BrS), 327 (1.25), 326 (5.0), 325 (5.0), 324 (5.0), 323 (5.0), 313 (1.25), 312 (17.5), 311 (60.25), 310 (25.00), 309 (1.24), 300 (1.25), 299 (1.25), 298 (5.0), 297 (2.5), 296 (1.25), 295 (7.5), 294 (5.0), 292 (2.5), 285 (1.25), 284 (2.5), 283 (7.5), 282 (2.5), 281 (5.0), 275 (1.25), 274 (5.0), 273 (15.00), 272 (5.0), 271 (7.50), 269 (2.5), 268 (2.5), 267 (1.25), 262 (2.5), 261 (11.25), 260 (2.5), 259 (2.5), 258 (1.25), 257 (1.25), 256 (0.62), 255 (1.25), 253 (0.62), 249 (2.5), 248
(5.0), 247 (7.50), 246 (10.00), 242/244 (2.5/2.8; C_{11}H_{17}NBr)
244 (2.5), 239 (2.5), 233 (2.5), 232 (10.00), 231 (37.5),
230 (37.5), 230 (5.0), 229 (7.5), 228 (2.5), 227 (1.25), 219
(5.0), 217 (2.5), 216 (1.25), 215 (1.25), 214 (2.5), 213 (5.0),
203 (17.5), 202 (5.0), 201 (17.5), 191 (2.5), 189 (5.0), 179
(12.5), 178 (2.5), 177 (7.5), 176 (5.0), 175 (7.5), 174 (2.5),
173 (3.75), 172 (1.25), 171 (2.5), 165 (7.5), 163 (10.0), 162
(7.5; C_{11}H_{16}N), 161 (7.5), 160 (1.25), 159 (5.0), 157 (2.5),
156 (2.5), 155 (1.25), 151 (1.25), 150 (10.00), 149 (30.0), 148
(15.00), 147 (20.00; C_{10}H_{13}N), 146 (5.0), 145 (7.5), 144 (2.5),
143 (2.5), 141 (1.25), 140 (2.5), 139 (1.25), 138 (2.5), 137
(5.0), 136 (10.0), 135 (50.00), 134 (40.00), 133 (11.25), 132
(20.00), 131 (5.0), 130 (2.5), 129 (5.0), 128 (2.5), 127 (1.25),
125 (2.5), 124 (5.0), 123 (40.00), 122 (11.23), 121 (7.5), 120
(2.5), 119 (2.5), 118 (2.5), 111 (5.0), 110 (5.0), 109 (15.0),
108 (30.00), 107 (80.00), 106 (100.00), 105 (97.5), 104 (12.5),
103 (1.25), 97 (5.0), 96 (5.0), 95 (42.5), 94 (12.5), 93 (35.0),
92 (10.0), 91 (27.5), 90 (25.0), 89 (27.5), 85 (2.57), 84 (2.5),
83 (5.0), 82 (5.0), 81 (27.5), 80 (7.5), 79 (25.0), 78 (2.5),
77 (12.5), 76 (12.5), 75 (80.00), 74 (55.0), 70 (5.0), 69 (22.5),
68 (10.0), 67 (27.5), 66 (2.5), 65 (2.75), 64 (2.75), 63 (2.5),
62 (15.0), 61 (15.0), 60 (75.00), 59 (90.00), 58 (15.00), 57
(25.0), 56 (7.5), 55 (27.5), 54 (5.0), 53 (7.5), 52 (2.5), 51
(7.5), 50 (2.5), 49 (2.5), 48 (37.5), 47 (25.0), 46 (15.0), 45
(62.5), 44 (20.0), 43 (97.50), 42 (27.5), 41 (30.00), 40 (30.00).
Reaction of 3β-bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVII) with chloroacetic acid and sodium acetate:

6'(7'H)-Oxospiro[3β-bromo-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXII)

3β-Bromo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVII) (2 g, 3.62 m mol), chloroacetic acid (1 g) and fused sodium acetate (0.9 g) were taken in anhydrous ethanol (50 ml) and the mixture was heated under reflux for 5 hrs. The semi-solid obtained after usual workup was recrystallized from ethanol to obtain 6'(7'H)-oxospiro[3β-bromo-5α-cholestan-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXII) (1.35 g, 2.28 m mol) m.p. 197º.

Analysis Found: C, 60.7; H, 8.0; N, 9.4

C₃₀H₄₉N₄BrOS requires: C, 60.7; H, 8.3; N, 9.4%.

IR: \(\nu_{\text{max}}\) 3420-3340 (N-H), 1725 (C=O), 1620 (C=N), 1480 (C-N) and 610 cm⁻¹ (C-Br).

¹H-NMR: \(\delta\) 5.5 (brs, 2X-N-H), 3.8 (mc, C3α-H, \(J_{2,2} = 14\) Hz, axial), 2.1 (s, 2H, CH₂CO), 1.2 (C10-CH₃), 0.70 (C13-CH₃), 0.91 and 0.81 (other methyl protons).

MS: 592/594 (C₃₀H₄₉N₄BrOS, absent), 512 (7.89), 467 (2.66), 466 (2.00), 450 (1.33), 439 (1.33), 438 (1.33; C₂₈H₄₆N₄), 399 (13.30), 384 (7.32), 370 (0.67), 369 (1.33), 368 (2.00), 341 (0.67), 340 (0.67), 325 (3.99), 310 (26.60), 270 (1.33), 269 (1.33), 264 (10.64), 263 (7.89), 262 (13.30), 261(100.00),
Reaction of 3β-iodo-5α-cholestan-6-one (CXIII) with thiocarbohydrazide: 3β-Iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII)

3β-Iodo-5α-cholestan-6-one (CXIII), (1 g, 2.02 m mol) was dissolved in ethanol (15 ml). To this a solution of thiocarbohydrazide (1 g, 9.40 m mol) in acetic acid (20 ml) was added over a period of 15 minutes. The mixture on usual workup gave 3β-Iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII) m.p. 156° (0.60 g, 1.00 m mol).
Analysis Found: C, 56.0; H, 8.0; N, 9.2

C$_{28}$H$_{49}$N$_4$I$_2$ requires: C, 56.0; H, 8.2; N, 9.3%.

IR: $\nu_{\text{max}}$, 3240 (N-H), 1640, 1520 (N-H), 1480 (C-N), 1080 (C=S) and 800 cm$^{-1}$ (C-I).

$^1$H-NMR: $\delta$ 5.3 (mc, 4X-N-H), 3.7 (mc, C3$\alpha$-H; $\omega_{1/2}$ = 18 Hz, axial), 1.2 (C10-CH$_3$), 0.75 (C13-CH$_3$), 0.90 and 0.80 (other methyl protons).

MS: 600 (C$_{28}$H$_{49}$N$_4$I$_2$, Absent), 512 (4.60; C$_{27}$H$_{47}$NI), 496 (4.6), 495 (81.65), 490 (4.60), 489 (2.30), 399 (3.45), 387 (2.30), 386 (13.80), 385 (52.90), 384 (9.20; C$_{27}$H$_{46}$N), 378 (6.9; C$_{12}$H$_9$N$_4$I$_2$), 370 (3.45), 369 (10.35; C$_{26}$H$_{43}$N), 368 (6.9), 367 (20.70), 366 (3.45), 356 (2.3), 327 (3.45), 325 (6.9), 324 (2.3), 311 (3.45), 310 (1.15), 290 (2.3; C$_{11}$H$_{17}$NI), 273 (3.45), 271 (1.15), 261 (1.15), 259 (2.3), 257 (1.15), 255 (3.45), 247 (3.45), 245 (3.45), 243 (1.15), 241 (2.3), 233 (2.3), 231 (3.45), 229 (3.45), 227 (1.15), 219 (1.15), 217 (2.3), 215 (3.45), 213 (1.15), 212 (1.15), 211 (2.3), 207 (1.15), 205 (1.15), 203 (2.3), 202 (2.3), 201 (1.15), 200 (1.15), 199 (1.15), 197 (2.30), 196 (1.15), 195 (1.15), 193 (2.3), 191 (2.3), 189 (9.2), 188 (20.7), 187 (4.6), 186 (2.3), 185 (2.3), 183 (1.15), 182 (1.15), 181 (1.15), 179 (6.9), 176 (2.3), 175 (6.9), 174 (2.3), 173 (9.2), 172 (2.3), 171 (1.15), 170 (1.15), 167 (2.3), 165 (1.15), 163 (1.15), 162 (9.2; C$_{11}$H$_{16}$N), 161 (4.6), 160 (6.9), 159 (11.50), 158 (2.3), 157 (3.45), 155 (1.15), 151 (2.3), 150 (2.3),
149 (11.5), 147 (18.4; C_{10}H_{13}N), 146 (51.45), 145 (9.2), 144 (6.9), 143 (3.94), 137 (4.6), 136 (6.9), 135 (16.1), 134 (6.9), 133 (27.6), 132 (11.5), 131 (18.4), 130 (4.02), 129 (2.3), 128 (6.9), 127 (2.3), 125 (3.45), 124 (2.3), 123 (16.1), 122 (6.9), 121 (20.7), 120 (11.5), 119 (13.8), 118 (11.5), 117 (6.9), 116 (1.15), 115 (9.2), 111 (5.75), 110 (3.45), 109 (11.5), 108 (8.05), 107 (23.0), 106 (100.00), 105 (9.2), 97 (4.6), 96 (32.2), 94 (6.9), 93 (18.4), 92 (1.15), 91 (13.8), 89 (3.45), 87 (1.15), 85 (1.15), 84 (1.15), 83 (9.2), 82 (2.3), 81 (23.0), 80 (3.45), 79 (16.1), 78 (1.15), 77 (6.9), 76 (35.80), 75 (6.9), 74 (6.9), 71 (11.5), 70 (1.15), 69 (16.1), 68 (4.6), 67 (36.8), 66 (1.15), 65 (2.3), 62 (2.3), 61 (3.45), 60 (59.0), 59 (36.8), 58 (6.9), 57 (29.9), 56 (9.2), 55 (34.5), 54 (2.3), 53 (2.3), 51 (1.15), 50 (1.15), 48 (11.5), 47 (6.9), 46 (5.75), 45 (24.15), 44 (4.6), 43 (6.7), 42 (18.4), 41 (23.00), 40 (24.15).

Reaction of 3β-iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII) with chloroacetic acid and sodium acetate:

6′(7'H)-Oxospiro[3β-iodo-5α-cholestan]-6,3′-(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXIII)

3β-Iodo-5α-cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione (CXVIII) (2 g, 3.33 m mol), chloroacetic acid (1 g) and fused sodium acetate (0.9 g) were taken in anhydrous ethanol (150 ml) and the mixture was heated under reflux for 5 hrs under the similar reaction conditions as described earlier. The semi-solid
thus obtained was recrystallized from ethanol to give 6'(7'H)-oxospiro[3β-iodo-5α-cholestan]-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (CXXIII) (1.29 g, 2.01 m mol) m.p. 181°.

Analysis Found : C, 56.1; H, 7.6; N, 8.6

C₃₀H₄₉N₄IOS requires : C, 56.3; H, 7.6; N, 8.8%

IR : 3400–3240 (N-H), 1740 (C=O), 1640 (C=N), 1500 (C-N) and 800 cm⁻¹ (C-I).

¹H-NMR : δ 5.6 (brs, 2X-N-H), 3.7 (mc, C3α-H; W½ = 14 Hz, axial), 2.0 (s, 2H, CH₂CO), 1.2 (C10-CH₃), 0.78 (C13-CH₃), 0.91 and 0.81 (other methyl protons).

MS : 640 (C₃₀H₄₉N₄IOS, absent), 512 (16.00), 504 (24.00), 500 (9.60), 499 (27.20), 498 (11.20), 497 (12.80), 491 (28.80), 490 (1.60), 488 (19.20), 487 (9.60), 486 (11.20), 480 (6.40), 479 (11.20), 474 (19.20), 470 (4.80), 465 (16.00), 458 (28.80), 457 (64.00), 456 (4.80), 446 (8.00), 445 (22.40), 444 (35.20), 438 (1.60; C₂₈H₄₆N₄), 437 (0.80), 428 (1.60), 427 (6.40), 426 (16.00), 424 (1.60), 422 (0.80), 421 (4.80), 420 (9.60), 419 (4.80), 418 (6.40), 417 (4.80), 405 (1.60), 404 (4.80), 403 (40.00), 402 (60.80), 401 (17.6), 400 (1.60), 399 (0.80), 390 (3.20), 389 (6.40), 388 (11.20), 387 (8.00), 386 (6.40), 385 (1.60), 384 (22.40)
372 (1.60), 371 (1.60), 370 (8.00), 369 (1.60), 368 (1.60),
359 (1.60), 357 (1.60), 356 (6.40), 355 (0.80), 347 (9.60),
331 (1.60), 328 (9.60), 325 (8.00), 312 (3.20), 310 (3.20), 298
(2.40), 297 (4.80), 296 (4.80), 295 (6.40), 272 (3.20), 271
(17.60), 270 (0.80), 266 (11.20), 264 (6.40), 256 (14.40), 253
(8.00), 251 (7.20), 250 (6.40), 239 (11.20), 230 (6.40), 226
(4.80), 225 (4.80), 210 (9.60), 208 (14.40), 207 (16.00), 206
(17.60), 201 (4.80), 195 (9.60), 194 (6.40), 193 (11.20), 191
(11.20), 190 (3.20), 182 (8.00), 181 (14.40), 177 (11.20), 175
(6.40), 170 (4.80), 169 (19.20), 168 (100.00), 167 (30.40), 166
(17.60), 165 (6.40), 164 (11.20), 163 (1.60), 154 (11.20), 153
(68.80), 152 (16.00), 151 (9.60), 150 (30.40), 148 (9.60), 140
(16.00), 139 (8.00), 138 (17.60), 136 (20.80), 135 (8.00), 134
(8.00), 130 (4.80), 128 (9.60), 126 (16.00), 124 (19.20), 122
(9.60), 115 (6.40), 114 (4.80), 112 (20.80), 110 (8.00), 109
(19.20), 99 (11.20), 98 (38.40), 95 (4.80), 94 (36.80), 88(11.20),
87 (7.20), 86 (32.00), 85 (11.20), 84 (33.60), 82 (35.20), 81
(4.80), 80 (12.80), 73 (35.20), 72 (9.60), 71 (46.40), 70 (8.00),
69 (35.20), 59 (3.20), 58 (64.00), 57 (12.80), 56 (88.00), 55
(4.80), 54 (6.40), 45 (3.20), 44 (49.60), 43 (62.40), 42 (9.60),
41 (72.00), 40 (67.20).

3β,5,6β-Trihydroxy-5α-cholestane

A mixture of cholesterol (20 g) and formic acid (20 ml;
88%) was heated on a water bath at 70-80° for 5 minutes and then
allowed to attain room temperature. Hydrogen peroxide (20 ml; 30%) was added to the mixture and it was kept at room temperature for 12 hrs with occasional shaking. Boiling water (300 ml) was added to the mixture with stirring and the reaction mixture was allowed to attain room temperature when a white solid separated which was filtered under suction and air-dried. The solid was dissolved in methanol (600 ml) and the solution was heated with sodium hydroxide solution (20 ml; 25%) for 10 minutes on a steam bath. It was acidified with hydrochloric acid and diluted with boiling water (300 ml). The triol obtained on cooling, was collected by filtration and recrystallized from methanol to give 3β,5,6β-trihydroxy-5α-cholestan (18 g) m.p. 237° (reported, m.p. 237-239°).

3β,5-Dihydroxy-5α-cholestan-6-one (CXXIV)

To a solution of 3β,5,6β-trihydroxy-5α-cholestan (10 g) in dioxane (90 ml) was added N-bromosuccinimide (4.5 g) at about 25°. After 15 minutes, the reaction mixture was cooled in an ice bath and the solid which crystallized out was collected by filtration under suction and washed thoroughly with 50% methanol to give dihydroxyketone (CXXIV), (6.5 g) m.p. 231° (reported, m.p. 231-233°).

3β-Acetoxy-5,6β-dihydroxy-5α-cholestan

3β-Acetoxy-5,6α-epoxy-5α-cholestan (8 g), was
dissolved in acetone (140 ml) and to this hydroiodic acid (16 ml) was added and the reaction mixture was refluxed for 1 hr. The progress of the reaction was monitored by TLC. After the completion of the reaction, the solvent was removed under reduced pressure and the residue obtained was extracted with ether. The ethereal extract was washed with water, sodium bicarbonate solution (5%) and again with water and was dried over anhydrous sodium sulphate. Evaporation of the ether gave semi-solid which was recrystallized from methanol to give 3β-acetoxy-5,6β-dihydroxy-5α-cholestane, m.p. 203° (reported, 203-205°).

3β-Acetoxy-5-hydroxy-5α-cholestan-6-one (CXXV)

I 3β-Acetoxy-5,6β-dihydroxy-5α-cholestane (4.0 g) was dissolved in acetone (30 ml) and was kept in ice bath. To this solution, Jone's reagent (35 g of chromium trioxide in 100 ml of water + 30 ml of H₂SO₄) was added dropwise with stirring till the colour of the solution persisted. The solution was further stirred for 30 minutes. The reaction mixture was diluted with water and the precipitated solid was filtered, dried and recrystallized from acetone to give the ketone (CXXV) (3.0 g) m.p. 232° (reported, 232-233°).

II A mixture of 3β,5-dihydroxy-5α-cholestan-6-one (CXXIV) (10 g)
pyridine (15 ml, freshly distilled over KOH) and acetic anhydride (10 ml) was heated under reflux for 2 hrs. The reaction mixture was allowed to cool at room temperature and treated with water. The reaction product consisting of colourless needles was filtered, washed with a little methanol and air-dried. Recrystallization from methanol gave the hydroxyketone (CXXV), (6.5 g), m.p. 232° (reported, 232-233°).

3β-Chloro-5,6β-dihydroxy-5α-cholestane

Finely powdered 3β-chlorocholest-5-ene (28 g) was dissolved in hot glacial acetic acid (300 ml) and treated with hydrogen peroxide (60 ml; 30%). The reaction mixture was kept at 95° for 1 hr. After removal of the solvent the oily product was extracted with ether and the ethereal layer was washed successively with water, sodium bicarbonate solution (10%) and water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil (≈ 12 g) which was chromatographed over silica gel (240 g) and eluted in 50 ml portions. Elution with petroleum ether - benzene (7:3) gave the unreacted 3β-chlorocholest-5-ene (2 g), m.p. 96° (reported, 96°). Further elution with benzene - chloroform (9:1) gave 3β-chloro-5-hydroxy-6β-acetoxy-5α-cholestane (3.31 g) m.p. 148° (reported, 150-151°).

Elution with chloroform gave 3β-chloro-5,6β-dihydroxy-5α-cholestane, recrystallized from methanol (2.3 g),
m.p. 124° (reported[^50], 126°, positive Beilstein test for halogen).

3β-Chloro-5-hydroxy-5α-cholestan-6-one (CXXVI)

3β-Chloro-5,6β-dihydroxy-5α-cholestane (2 g) was dissolved in ether (40 ml), methanol (10 ml) and water (10 ml) and treated with N-bromosuccinimide (1 g). After 1 hr, ether (50 ml) was added and the solution was washed with water, sodium metabisulphite solution (10%) and water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave the crude ketone (CXXVI) which was recrystallized from acetone to afford 3β-chloro-5-hydroxy-5α-cholestan-6-one (CXXVI), (1.4 g), m.p. 181° (reported[^50], 182°).

Reaction of 3β,5-hydroxy-5α-cholestan-6-one (CXXIV) with benzoic hydrazide: 3β-Hydroxy-5α-cholestanol(6,5-c)-oxazetene (CXXVII)

A mixture of 3β,5-hydroxy-5α-cholestan-6-one (CXXIV) (2.0 g, 4.78 m mol) and benzoic hydrazide (2.0 g) in dry ethanol (50 ml) containing glacial acetic acid (5 ml) was heated under reflux on a water bath for 6 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into ice-cold water and the precipitated compound was filtered and dried. It was recrystallized from acetone to provide 3β-hydroxy-5α-cholestanol(6,5-c)-oxazetene (CXXVII) (1.50 g, 3.61 m mol), m.p. 138°.
Analysis Found: C, 78.01; H, 10.91; N, 3.37

C₂₇H₄₅NO₂ requires: C, 78.00; H, 10.90; N, 3.40%

IR: \( \nu_{\text{max.}} \) 3400 (\(-\text{OH}\)), 1630 (C=N), 1020 (C-O) and 950 cm\(^{-1}\) (N-O).

\(^1\text{H-NMR}\): \( \delta \) 3.6 (mc, 1H, \( J = 18 \text{ Hz} \); C₃α-H); 1.2 (C₁₀-CH₃), -0.75 (C₁₃-CH₂). 0.91 and 0.85 (other methyl protons).

\( ^1\text{H-NMR} \): \( \delta \) 3.6 (mc, 1H, \( J = 18 \text{ Hz} \); C₃α-H); 1.2 (C₁₀-CH₃), 0.91 and 0.85 (other methyl protons).

MS: 415 (1.43; C₂₇H₄₅O₂N), 400 (5.72), 398 (0.72), 397 (2.15; C₂₇H₄₃ON), 391 (0.72), 390 (5.72), 389 (36.00), 388 (100.00), 387 (97.14), 386 (98.53), 384 (4.29), 383 (4.29), 382 (0.72), 381 (1.43), 374 (2.86), 373 (14.30), 372 (45.76), 371 (5.72), 370 (15.73), 369 (71.50), 368 (4.29), 367 (2.86; 397-NO), 366 (0.72), 365 (0.72), 361 (0.72), 360 (1.43), 359 (1.43), 358 (2.86), 357 (1.43), 356 (4.29), 355 (17.16), 354 (54.34), 352 (1.43), 351 (0.72), 345 (0.72), 343 (1.43), 342 (2.86), 341 (2.86), 340 (0.72), 339 (1.43), 338 (1.43), 332 (0.72), 330 (4.29), 329 (8.58), 328 (2.86), 327 (8.58), 326 (11.44), 325 (1.43), 316 (0.72), 315 (1.43), 314 (2.86), 313 (4.29), 312 (0.72), 311 (2.86), 310 (0.72), 303 (2.86), 302 (17.16), 301 (97.14), 300 (4.29), 299 (1.43), 298 (0.72), 292 (0.72), 290 (0.72), 288 (1.43), 267 (1.43), 262 (2.86), 261 (7.15), 260 (7.15), 248 (8.58), 247 (20.18), 246 (8.58), 245 (5.72), 240 (7.15), 239 (1.43), 238 (2.15), 235 (0.72), 233 (5.72), 232 (8.58), 230 (2.86), 229 (14.30), 228 (14.30), 227 (8.58), 216 (11.44), 215 (14.30), 211
Reaction of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (CXXV) with benzoic hydrazide: 3β-Acetoxy-5α-cholestan-6-one (CXXV) (2.0 g, 4.34 mmol)
dissolved in dry ethanol (50 ml) was treated with benzoic hydrazide (2.0 g) and glacial acetic acid (5 ml). The reaction mixture was kept under reflux for 6 hrs and poured in to ice-cold water. The precipitated solid was filtered air dried and was recrystallized from methanol to provide 3β-acetoxy-5α-cholestan-6,5-c-oxazetene (CXXVIII) (1.6 g, 3.49 mmol), m.p. 161°.

Analysis Found: C, 76.09; H, 10.36; N, 3.60

C<sub>29</sub>H<sub>47</sub>NO<sub>3</sub> requires: C, 76.10; H, 10.40; N, 3.60%

IR: ν<sub>max.</sub> 1735 (CH<sub>3</sub>COO<sup>-</sup>), 1610 (C=N), 1460, 1240 (C-O), 1050 (C-O) and 950 cm<sup>-1</sup> (N-O).

<sup>1</sup>H-NMR: δ 4.02 (mc, 1H, J<sub>1/2</sub> = 18Hz; C3α-H), 2.0 (s, 3H, CH<sub>3</sub>COO<sup>-</sup>), 1.15 (C10-CH<sub>3</sub>), 0.75 (C13-CH<sub>3</sub>), 0.95 and 0.85 (other methyl protons).

MS: 457(M<sup>+</sup> 2.94; C<sub>29</sub>H<sub>47</sub>NO<sub>3</sub>), 442 (2.21), 440 (0.74), 439 (2.94), 431 (0.74), 430 (1.47), 429 (1.47), 422 (1.47), 421 (4.41), 420 (14.70), 419 (51.45), 418 (2.21), 417 (0.74), 416 (1.47), 415 (4.41), 414 (2.21), 413 (4.41), 412 (2.94), 411 (1.47), 410 (4.41), 404 (1.47), 403 (4.41), 402 (7.35), 401 (19.11), 400 (4.41), 399 (5.88), 398 (7.35), 397 (5.88; C<sub>27</sub>H<sub>43</sub>NO), 396 (4.41), 395 (4.41), 394 (1.47), 393 (0.74), 392 (0.74), 391 (0.74), 390 (0.74), 389 (1.47), 388 (2.21), 387 (4.41), 386 (7.35), 385 (5.88), 384 (5.88), 383 (8.82), 382 (4.41), 381 (4.41), 380 (1.47), 379 (0.74), 374 (4.41), 373 (5.88),...
372 (2.94), 371 (4.41), 370 (4.41), 369 (5.88), 368 (4.41), 367 (4.41; C_27H_{43}), 366 (4.41), 365 (4.41), 364 (0.74), 360 (4.41), 359 (8.82), 358 (4.41), 357 (5.88), 356 (4.41), 355 (0.74), 354 (0.74), 349 (2.94), 348 (7.35), 347 (1.47), 346 (2.94), 345 (4.41), 344 (8.82), 343 (1.47), 342 (0.74), 341 (2.94), 335 (0.74), 334 (2.94), 333 (4.41), 332 (2.94), 331 (1.47), 330 (1.47), 329 (0.74), 328 (1.47), 327 (0.74), 326 (0.74), 321 (2.94), 320 (11.76), 319 (47.04), 318 (7.35), 317 (2.94), 316 (2.94), 315 (2.94), 314 (2.94), 310 (0.74), 306 (1.47), 305 (2.94), 304 (8.82), 303 (1.47), 302 (2.21), 301 (0.74), 300 (0.74), 299 (0.74), 290 (2.94), 289 (2.94), 288 (4.41), 287 (1.47), 279 (2.94), 278 (1.47), 274 (2.94), 270 (4.41), 264 (2.94), 263 (2.21), 262 (4.41), 261 (4.41), 260 (4.41), 259 (2.21), 250 (1.47), 249 (4.41), 248 (11.76), 247 (7.35), 246 (10.29), 245 (1.47), 244 (2.94), 243 (2.94), 242 (2.21), 241 (2.21), 240 (0.74), 239 (0.74), 238 (0.74), 234 (4.41), 233 (4.41), 232 (5.88), 231 (1.47), 230 (5.88), 229 (4.41), 228 (7.35), 227 (1.47), 226 (2.21), 220 (4.41), 219 (2.94), 218 (7.35), 217 (2.94), 216 (4.41), 215 (2.94), 214 (4.41), 213 (2.21), 212 (2.94), 211 (0.74), 210 (1.47), 209 (0.74), 208 (2.94), 207 (4.41), 206 (4.41), 205 (2.21), 204 (5.88), 203 (2.94), 202 (5.88), 201 (2.94), 200 (5.88), 199 (0.74), 198 (2.21), 197 (2.21), 196 (2.21), 194 (4.41), 193 (2.94), 192 (5.88), 191 (2.94), 190 (8.82), 189 (4.41), 188 (5.88), 187 (2.94), 186 (5.88), 185 (0.74), 184 (2.94),
183 (1.47), 182 (1.47), 181 (1.47), 180 (4.41), 179 (5.88), 178 (7.35), 177 (5.88), 176 (10.29), 175 (7.35; C_{11}H_{13}NO), 174 (13.23), 173 (2.94), 172 (4.41), 171 (2.94), 170 (4.41), 169 (0.74), 168 (0.74), 167 (0.74), 166 (2.94), 165 (2.94), 164 (11.76), 163 (7.35), 162 (16.17), 161 (8.82), 160 (9.56; C_{10}H_{10}NO), 159 (2.94), 158 (4.41), 157 (2.21), 156 (2.21), 154 (4.41), 153 (7.35), 152 (5.88), 151 (4.41), 150 (13.23), 149 (10.29), 148 (13.23), 147 (5.88), 146 (10.29), 145 (2.94), 144 (4.41), 143 (2.94), 142 (2.94), 141 (2.21), 140 (8.82), 139 (2.94), 138 (10.29), 137 (16.17), 136 (17.64), 135 (10.29), 134 (17.64), 133 (4.41), 132 (7.35), 131 (1.47), 130 (4.41), 129 (11.76), 128 (5.88), 127 (2.94), 126 (4.41), 125 (4.41), 124 (14.70), 123 (29.40), 122 (89.67), 121 (8.82), 120 (13.23), 119 (2.94), 118 (2.94), 117 (1.47), 116 (2.21), 115 (0.74), 114 (2.94), 113 (2.94), 112 (13.23), 111 (41.16), 110 (22.05), 109 (11.76), 108 (24.99), 107 (23.52), 106 (100.00), 105 (2.94), 104 (4.41), 103 (0.74), 102 (0.74), 101 (0.74), 100 (4.41), 99 (2.94), 98 (11.76), 97 (8.82), 96 (33.81), 95 (11.76), 94 (27.93), 93 (5.88), 92 (16.17), 91 (0.74), 90 (0.74), 89 (0.74), 88 (0.74), 87 (0.74), 86 (7.35), 85 (5.88), 84 (41.16), 83 (10.29), 82 (33.81), 81 (4.41), 80 (17.64), 79 (14.70), 78 (98.53), 77 (7.35), 76 (4.41), 75 (5.88), 74 (2.94), 73 (2.21), 72 (17.64), 71 (4.41), 70 (29.40), 69 (10.29), 68 (22.05), 67 (2.21), 66 (4.41), 65 (0.74), 64 (2.21), 63 (1.47), 62 (1.47), 61 (1.47), 60 (0.74), 59 (33.81), 58 (7.35), 57 (44.10), 56 (2.94), 55 (5.88), 54 (0.74), 53 (5.88), 52 (36.75), 51 (14.70),
50 (1.47), 48 (2.94), 47 (0.74), 46 (4.41), 45 (19.11), 44 (55.86), 43 (4.41), 42 (32.34), 41 (16.17), 40 (8.82).

Reaction of 3β-chloro-5-hydroxy-5α-cholestan-6-one (CXXVI) with benzoic hydrazide: 3β-Chloro-5α-cholestan[6,5-c]-oxazetene (CXXIX)

3β-Chloro-5-hydroxy-5α-cholestan-6-one (CXXVI) (2.0 g, 4.20 m mol) was treated with benzoic hydrazide (2.0 g) in dry ethanol (50 ml) and glacial acetic acid (5 ml) was added and it was refluxed for 6 hrs. Usual workup of the mixture the solid compound obtained as earlier was recrystallized from acetone to afford 3β-chloro-5α-cholestan[6,5-c]-oxazetene (CXXIX) (1.58 g, 3.63 m mol), m.p. 113°.

Analysis Found: C, 74.70; H, 10.22; N, 3.22
C_{27}H_{44}NOCl requires: C, 74.70; H, 10.20; N, 3.20%

IR: \( \nu_{\text{max}} \) 1590 (C=N), 1010 (C=O), 920 (N-O), and 720 cm\(^{-1}\) (C-Cl) (positive Beilstein test).

\( ^1H\)-NMR: \( \delta \) 3.4 (mc, 1H, \( \beta = 16 \) Hz; C3α-H), 1.15 (C10-CH\(_3\)), 0.70 (C13-CH\(_3\)), 0.95 and 0.85 (other methyl protons).

MS: 433/435 (4.41/1.47; C\(_{27}\)H\(_{44}\)ONCl), 418/420 (10.29/3.4), 414 (1.47), 413 (2.21), 412 (7.40), 411 (0.74), 410 (0.74), 397 (2.21; C\(_{27}\)H\(_{43}\)NO), 392 (1.47), 391 (1.47), 390 (4.41), 389 (5.88), 388 (29.40), 386 (24.98), 385 (100.00), 384 (7.35), 383 (10.29), 382 (2.94), 381 (7.35), 373 (1.47), 372 (10.29), 371 (29.40), 370 (7.35), 369 (32.34), 368 (29.40), 367 (94.08), 366 (4.41), 365 (2.94), 359 (1.47),
358 (1.47), 357 (2.21), 356 (1.47), 355 (4.41), 354 (13.23), 353 (48.51), 352 (0.74), 351 (1.47), 350 (0.74), 344 (1.47), 343 (1.47), 342 (0.74), 341 (1.47), 340 (1.47), 332 (0.74), 331 (1.47), 330 (2.94), 329 (5.88), 328 (2.94), 327 (7.40), 326 (8.82), 325 (1.47), 320/322 (5.88/1.62), 318 (0.74), 317 (0.74), 316 (2.94), 315 (2.94), 314 (4.41), 312 (4.41), 311 (1.47), 310 (2.94), 307 (0.74), 306 (1.47), 305 (0.74), 304 (1.47), 303 (11.76), 302 (44.10), 301 (4.41), 300 (1.47), 299 (0.74), 298 (0.74), 291 (5.88), 290 (0.74), 289 (0.74), 288 (0.74), 287 (1.47), 286 (2.94), 285 (0.74), 282 (2.94), 280 (0.74), 278 (1.47), 277 (2.94), 276 (16.17), 275 (70.56), 274 (22.10), 273 (23.57), 272 (2.94), 271 (4.41), 270 (0.74), 269 (2.94), 268 (0.74), 267 (0.74), 266 (0.74), 265 (1.47), 264 (1.47), 263 (1.47), 262 (4.41), 261 (7.35), 260 (11.76), 259 (5.88), 257 (4.41), 256 (7.35), 255 (20.58), 251 (2.94), 250 (2.94), 249 (7.35), 248 (7.35), 247 (13.23), 246 (8.82), 245 (5.88), 241 (5.88), 240 (0.74), 239 (1.47), 233 (5.88), 232 (7.35), 231 (22.10), 230 (2.94), 229 (11.76), 228 (11.76), 227 (7.35), 226 (0.74), 225 (0.74), 220 (4.41), 219 (5.88), 218 (1.47), 217 (5.88), 216 (2.94), 215 (11.76), 214 (14.70), 213 (44.10), 212 (2.21), 211 (2.21), 210 (0.74), 209 (0.74), 208 (1.47), 207 (5.88), 206 (7.35), 205 (7.35), 204 (1.47), 203 (4.41), 202 (2.94), 201 (9.29), 200 (5.88), 199 (27.64), 198 (1.47), 197 (4.41), 196 (2.94), 195 (2.94), 194 (2.94), 193 (7.35), 192 (2.94), 191 (7.35), 190 (2.21), 189 (7.35), 188 (4.41), 187 (16.17), 186 (7.35), 185 (14.70), 184 (0.74),
179 (8.82), 178 (14.70), 177 (8.82), 176 (4.41), 175 (11.76; 
C_{11}H_{13}NO), 174 (17.14), 173 (29.40), 172 (5.88), 171 (14.70), 
170 (1.47), 169 (4.41), 168 (0.74), 167 (0.74), 165 (7.35), 
164 (5.88), 163 (29.40), 162 (8.82), 161 (44.10), 160 (17.14; 
C_{10}H_{10}NO), 159 (42.63), 158 (17.14), 157 (14.70), 156 (2.94), 
155 (2.94), 154 (0.74), 153 (1.47), 152 (4.41), 151 (10.29), 
150 (5.88), 149 (23.55), 148 (13.23), 147 (45.57), 146 (17.14), 
145 (61.74), 144 (10.29), 143 (23.55), 142 (2.94), 141 (2.94), 
140 (2.94), 137 (10.29), 136 (11.76), 135 (38.22) 
134 (14.70), 133 (44.10), 132 (11.76), 131 (29.40), 130 (7.35), 
129 (11.76), 128 (5.88), 127 (1.47), 126 (0.74), 125 (11.76), 
124 (8.82), 123 (22.10), 122 (45.57), 121 (35.28), 120 (42.63), 
119 (10.29), 118 (20.58), 117 (2.94), 116 (5.88), 115 (0.74), 
114 (2.94), 113 (2.94), 111 (14.70), 110 (8.82), 109 (42.63), 
108 (20.58), 107 (74.97), 106 (20.58), 105 (95.59), 104 (4.41), 
103 (4.41), 98 (2.94), 97 (2.21), 96 (20.58), 95 (8.82), 94 
(73.50), 93 (19.11), 92 (60.27), 91 (44.10), 90 (0.74), 85 (8.82), 
84 (2.94), 83 (32.34), 82 (11.76), 81 (76.44), 80 (8.82), 79 
(41.16), 78 (7.35), 77 (44.16), 76 (1.47), 72 (2.21), 71 (32.34), 
70 (5.88), 69 (55.86), 68 (10.29), 67 (49.98), 66 (2.94), 65 
(5.88), 58 (4.41), 57 (74.97), 56 (10.29), 55 (88.20), 54 (2.94), 
53 (11.76), 52 (1.47), 51 (10.29), 50 (4.41), 43 (5.88), 42 
(7.35), 41 (97.06), 40 (10.29),
References


Part Two

A Syntheses of Steroidal Thiocarboxylic Ketoxime Anhydrides
Theoretical

A - SYNTHESES OF STEROIDAL THIOCARBOXYLIC KETOXIME ANHYDRIDES

Nitroolefins act as the versatile synthetic intermediates. In recent past, much efforts are being made by organic chemists to synthesize a number of cyclic and open chain organic compounds by using these intermediates as starting materials. Corey and coworker reported the reactions of cyclonitroolefin (I) with different reagents and obtained (II-XI) as the products.

\[ \text{NO}_2 ] (I) \rightarrow \text{NH}_4\text{OH}, \text{THF} \rightarrow 45^\circ, 24 \text{ hrs.} \]
\[ \text{NaCN} \text{, MeOH} \rightarrow HCl, 0^\circ, 15 \text{ hrs.} \]
\[ \text{KoBu} \text{, BuOH} \rightarrow \text{THF} / \text{H}_2\text{SO}_4 \]
\[ \text{C}_5\text{H}_{11}\text{ONO}_2 \rightarrow \text{NaNO}_2, 25^\circ, 2 \text{ hrs.} \]

(II) \hspace{2cm} (III) \hspace{2cm} (IV) \hspace{2cm} (V)
It has been found\(^2,^3\) that hydrogen replaces the nitro group from the compounds such as (XII) and (XIII) on treatment with sodium salt of methyl mercaptan and obtained (XIV) and (XV) as the product respectively.
Krasuska et al.\textsuperscript{4} reported the reaction of 5-nitro-1,3-dioxanes (XVI) with potassium hydroxide - ethylene glycol and obtained 1,3-dioxanes (XVII - XVIII) as the products.

\begin{align*}
\text{R} & \quad \text{NO}_2^+ \\
\text{O} & \quad \text{O} \\
\text{(XVIa) CH}_3 & \quad \text{(XVIIa) CH}_3 & \quad \text{(XVIIIa) H} \\
\text{(XVIb) C}_2\text{H}_5 & \quad \text{(XVIIb) C}_2\text{H}_5 & \quad \text{(XVIIIb) CH}_3 \\
\text{(XVIc) n-C}_3\text{H}_7 & \quad \text{(XVIIc) n-C}_3\text{H}_7 & \quad \text{(XVIIIc) C}_2\text{H}_5 \\
\text{(XVID) n-C}_4\text{H}_9 & \quad \text{(XVID) n-C}_4\text{H}_9 & \quad \text{(XVIIIId) C}_3\text{H}_7
\end{align*}
Kornblum and Erickson\textsuperscript{5} reported the conversion of nitro compound (XIX) into aldehyde (XXI) through the compound (XX).

\[
\begin{align*}
\text{H}_3\text{C} & \begin{array}{c} \text{O} \end{array} \text{CH}_3 & \begin{array}{c} \text{C} \end{array} \text{CH}_3 & \begin{array}{c} \text{CH}_3 \end{array} & \begin{array}{c} \text{NO}_2 \end{array} \\
\text{H}_3\text{C} & \begin{array}{c} \text{O} \end{array} & \text{CH}_3 & \text{CH}_3 & \text{CH}_3
\end{align*}
\]

\[\text{Na}^+ \text{CH}_2\text{NO}_2 \xrightarrow{\text{NaOH, Me}_2\text{SO, 25°C}}\]

\[
\begin{align*}
\text{H}_3\text{C} & \begin{array}{c} \text{O} \end{array} \text{CH}_3 & \begin{array}{c} \text{C} \end{array} \text{CH}_3 & \begin{array}{c} \text{CH}_3 \end{array} & \begin{array}{c} \text{O} \end{array} \text{CH}_3 & \begin{array}{c} \text{C} \end{array} \text{CH}_3 & \begin{array}{c} \text{CH}_3 \end{array} & \begin{array}{c} \text{CH}_3 \end{array} & \begin{array}{c} \text{CH}_3 \end{array} & \begin{array}{c} \text{H} \end{array}
\end{align*}
\]

(XXI)

Blank and Fox\textsuperscript{6} reported that the treatment of 5-nitropyrimidines (XXII, XXIII) and 5-nitrocytidine (XXIV) with sodium azide leads to a novel and easy synthesis of 2-oxo-8-azapurine (XXV).

\[
\begin{align*}
\text{R} & \begin{array}{c} \text{O} \end{array} \text{NO}_2 \xrightarrow{\text{NaN}_3/DMF} \\
\text{R} & \begin{array}{c} \text{N} \end{array} \begin{array}{c} \text{H} \end{array} \begin{array}{c} \text{H} \end{array} \begin{array}{c} \text{R} \end{array} & \begin{array}{c} \text{N} \end{array} \begin{array}{c} \text{R} \end{array} \begin{array}{c} \text{NH}_2 \end{array} \begin{array}{c} \text{H} \end{array} \\
\text{R} & \begin{array}{c} \text{N} \end{array} \begin{array}{c} \text{H} \end{array} \begin{array}{c} \text{R} \end{array} \begin{array}{c} \text{NH}_2 \end{array} & \begin{array}{c} \text{NO}_2 \end{array} \text{DMF} \\
\text{R} & \begin{array}{c} \text{N} \end{array} \begin{array}{c} \text{H} \end{array} \begin{array}{c} \text{R} \end{array} & \begin{array}{c} \text{NH}_2 \end{array} \begin{array}{c} \text{NO}_2 \end{array} \text{DMF}
\end{align*}
\]

(XXV)
Gilsdrof and Nord\textsuperscript{7} showed lithium aluminium hydride reduction of l-phenyl-2-nitropropane (XXVI) followed by hydrolysis with an aqueous sodium or potassium tartrate solution to give β-phenylisopropylamine (XXVII). Literature survey\textsuperscript{8,9} also revealed the reduction of α,β-unsaturated nitro derivative (XXVIII) to yield (XXIX).

\[ \text{H}_5\text{C}_6 - \text{CH}_2 - \text{C} = \text{NO}_2 \xrightarrow{\text{LiAlH}_4} \text{H}_5\text{C}_6 - \text{CH}_2 - \text{CH} - \text{NH}_2 \]

(XXVI) \hspace{1cm} (XXVII)

\[ \text{H}_5\text{C}_6 - \text{CH} = \text{CH} - \text{NO}_2 \xrightarrow{\text{LiAlH}_4} \text{H}_5\text{C}_6\text{CH}_2\text{CH}_2\text{NH}_2 \]

(XXVIII) \hspace{1cm} (XXIX)

Kinstle and Stam\textsuperscript{10} reported that α,β-unsaturated nitro compound (XXX) on photochemical rearrangement provided benzophenone (XXXI) and isocyanate (XXXII) as products.

\[ \begin{array}{c}
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{NO}_2
\end{array} \xrightarrow{} \begin{array}{c}
\text{Ph} \\
\text{C} = \text{C} \\
\text{Ph} \\
\text{Ph}
\end{array} + \begin{array}{c}
\text{Ph} \\
\text{N} = \text{C} = \text{O}
\end{array} \]

(XXX) \hspace{1cm} (XXXI) \hspace{1cm} (XXXII)

It has been found that\textsuperscript{11,12,13} the irradiation of
3β-acetoxy-6-nitrocholest-5-ene (XXXIII) in hexane gave 6β-nitrocholest-4-en-3β-yl acetate (XXXIV) along with other products (XXXV), (XXXVI) and (XXXVII).

Hassner and Heathcock\textsuperscript{14} treated 3β-acetoxy-5α-chloro-6-nitrocholestane (XXXVIII) with chromium (II) chloride in methanoic hydrochloric acid to obtain 3β-acetoxy-5α-methoxy-6-oximinocholestane (XXXIX) whereas 3β-acetoxy-6-nitroandrost-17-one (XL) was reduced by sodium borohydride to 6α-nitroandrostane-3β,17β-diol (XLI).
Hanson and Premuzic\textsuperscript{15} treated $3\beta$-acetoxy-$6$-nitrocholest-$5$-ene (XXXIII) with chromium (II) chloride for 3 hours to obtain the oxime (XLII). Hanson and Organ\textsuperscript{16} also reported that, the reaction of $3\beta$-acetoxy-$6\beta$-nitro-$5\alpha$-cholestane (XLIII) under nitrogen with acidic chromium (II) chloride gives $3\beta$-acetoxy-$6$-oximino-$5\alpha$-cholestane (XLIV). $3\beta$-Acetoxy-$17\beta$-nitroandrost-$5$-ene (XLV) under similar reaction conditions provided oxime (XLVI), and $3,3$-dinitro-$5\alpha$-cholestane (XLVII) afforded oxime (XLVIII)\textsuperscript{17}. 
In contrast, the unsaturated nitro steroids such as 3β-acetoxy-6β-nitrocholest-4-ene (XXXIII) afforded the 6-ketone (XLIX) when treated with chromium (II) chloride while corresponding analogue (L) gave cholest-4-en-3-one (LI) whereas 6α- and 6β-nitrocholest-4-en-3-one (LII) furnished 5α-cholestane-3,6-dione (LIII).
Komeichi et al.\textsuperscript{19} found that the treatment of 6-nitrocholest-5-enes (XXXIII, LIV, LV) with dry hydrogen halide provided corresponding 5\(\alpha\)-halo-6-oximino-5\(\alpha\)-cholestanes (LVI - LIX).
Sato and coworkers reported the reduction of $3\beta$-acetoxy-6-nitrocholest-5-ene (XXXIII) which gave a 3,3'-dimer (LX) whereas 33-tosylate (LXI) gave $6\beta$-nitro-3α,5-cyclo-5α-cholestane (LXII). $3\beta$-Trifluoroacetate (LXIII) showed intermediate behaviour and gave both (LX) and (LXII) but (LXIV) gave 5β,19-cyclo-6-nitro steroid (LXV).
Stiver and Yates\textsuperscript{21} reported that treatment of 3β-acetoxy-6-nitrocholest-5-ene (XXXIII) with an excess of lithium dimethyl cuprate gave 3α,5-cyclo-5α-cholestan-6-one oxime (LXVI) and electrolysis of the tosylate (LXI) provided (LXII).
Pinhey and Smith\textsuperscript{22} noted that the treatment of 6β-nitrocholest-4-ene (LXVII) with catalytic amount of sodium methoxide in methanol gave an equilibrium mixture which contained the starting material (LXVII) and the 6α-epimer (LXVIII) in 1:1 ratio. According to them 6α-nitrosteroid is thermodynamically more stable than its 6β-epimer.
The formation of cyanosteroids (LXIX - LXXV) was reported when nitro steroids (L, XXXIII, LIV and LV) were treated with potassium cyanide in ethanolic ether (3:2).

\[
\begin{align*}
\text{R} & \quad \text{OH} \\
(\text{XXXIII}) & \quad \text{OAc} \\
(\text{LIV}) & \quad \text{Cl} \\
(\text{LV}) & \quad \text{H}
\end{align*}
\]
Barton et al. reported\textsuperscript{24} the reduction of nitro compounds (LXXVI-a, LXXVII-a, LXXVIII, LXXX, LXXXII and LXXXIV) to oximes (LXXVI-b, LXXVII-b, LXXIX, LXXXI, LXXXIII and LXXXV) when treated with triethylamine and carbon disulphide.
The reaction of 3α,4α-epoxy-6-nitrocholest-5-ene (LXXXVI) with phenyl isocyanate or acrylamide afforded 3α,4β-dihydroxy-6-nitrocholest-5-ene (LXXXVII) and 6-nitrocholest-5-en[3α,4α-δ]oxazolidin-2'-one (LXXXVIII) as the products\textsuperscript{25}.

\[
\text{C}_9\text{H}_{17}\text{PhNCO/CH}_2\text{=CHCONH}_2\text{AlCl}_3, \text{DMF}
\]

The reaction\textsuperscript{26} of steroidal nitroolefins (XXXIII, LIV and LV) with methylamine in the presence of zinc-dust afforded steroidal ketoximes (XLIV, LXXXIX and XC).
The reactions of steroidal nitroolefins (XXXIII, LIV, LV and XCI) with sodium methoxide and acetonitrile gave isomerized nitroolefins (XXXIV, XCII, XCI and XCIV) whereas nitroolefins (XXXIII, LIV and XCI) over basic silica gel provided 6-nitrocholesta-3,5-diene (XXXVII) and 3β-hydroxycholest-4-en-6-one (XCV) as products.
The reaction of 6-nitrocholesta-3,5-diene (XXXVII) with perbenzoic acid afforded 3α,4α-epoxy-6-nitrocholest-5-ene (LXXXVI) which on treatment with acrylonitrile in presence of boron trifluoride (BF₃:Et₂O, dry) gave (XCVI) and (XCVII) as the products.²⁹
The chromic acid oxidation of steroidal nitroolefin (XXXVII) and bromonitroolefins (XCVIII) afforded (XCIX), (C), (CI), (CII), (CIII), (CIV) and (CV) as the products.\(^{30}\)
The reaction of nitroolefins (LIV) with lead tetra acetate afforded (CVI), (CVII) and (CVIII) as the products\textsuperscript{31}. 

\[ \text{C}_9\text{H}_7\text{Pb(OAc)}_4 \text{AcOH, CH}_3\text{COOH} \] 

(LIV) + (LIV) + (CVI) + (CVII) + (CVIII)
Discussion

Several papers dealing with the reactions of steroidal vinyl nitro derivatives have appeared from our laboratories. In the present work, an attempt has been made to prepare steroidal compounds incorporating carbon nitrogen and sulphur linkages.

Recently, Barton and coworkers have reported a mild procedure for the reduction of aliphatic nitro compounds to oximes in which they used carbon disulphide in the presence of triethylamine. We have also followed the same procedure with some steroidal nitroolefins such as (LV, XXXIII and LIV) in anticipation of obtaining the corresponding oximes which could be further utilized for Beckmann rearrangement. Surprisingly enough, in place of oximes we obtained the cyclized thiocarboxylic ketoxime anhydrides (CIX – CXI) in good yields.

The reaction of steroidal nitroolefins (LV, XXXIII and LIV) with carbon disulphide in triethylamine, acetonitrile afforded 6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CIX), 3β-acetoxy-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CX) and 3β-chloro-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CXI), respectively.
Reaction of 6-nitrocholest-5-ene (LV) with carbon disulphide in triethylamine acetonitrile: 6-Oximinocholest-4-ene-4-thio-carboxylic anhydride (CIX)

To a stirred solution of the nitroolefins (LV) (2.0 g, 4.98 mmol) in acetonitrile (15 ml) was added triethylamine (4.5 g, 44.5 mmol) followed by carbon disulphide (0.91 g, 12 mmol). The mixture was stirred at room temperature for 72 hrs and then concentrated under reduced pressure and the residue was extracted with dichloromethane and washed with water, sodium hydrogen carbonate solution (5%) and again with water. The organic layer was dried over anhydrous sodium sulphate. The solvent was evaporated and the residue was chromatographed over a neutral
alumina column to afford the product (CIX) which was recrystallized from methanol m.p. 110°.

Characterization of the compound, m.p. 110° as 6-oximinocholesten-4-ene-4-thiocarboxylic anhydride (CIX):

The compound, m.p. 110° was correctly analysed for C_{28}H_{43}NO_{3}. Its IR spectrum exhibited bands at 1650 (C=N), 1640 (C=C), 1080 (C=S), 1020 (C=O) and 815 cm^{-1} (N=O). In the ^1H-NMR spectrum of the compound only the angular and side chain methyl protons were observed at δ 1.20 (C_{10}-CH_{3}), 0.68 (C_{13}-CH_{3}), 0.90 and 0.80 (other methyl protons). Thus in the light of above discussion the compound, m.p. 110° was characterized as 6-oximinocholesten-4-ene-4-thiocarboxylic anhydride (CIX). This structure was further supported by its mass spectral studies. The mass spectrum of the compound (CIX) showed prominent fragment ions at m/z 397, 382, 381, 367, 328, 284, 268, 254, 253, 239 and lower ion peaks. Tentative pathways for the formation of some of the significant
ions are given in Scheme-1.

\[ \text{SCHEME-1} \]

**Reaction of 3β-acetoxy-6-nitrocholest-5-ene (CXXXIII) carbon disulphide in triethylamine acetonitrile:** 3β-Acetoxy-6-oximinocholest-4-ene-thiocarboxylic anhydride (CX)

The 3β-acetoxy-6-nitrocholest-5-ene (XXXIII) (2.0 g, 4.10 m mol) in acetonitrile (15 ml) and triethylamine (4.5 g, 44.5 m mol) followed by carbon disulphide (0.91 g, 12 m mol) addition under the similar reaction conditions and usual workup as mentioned in the earlier reaction afforded the product (CX), m.p. 116°.
Characterization of the compound, m.p. 116° as 3β-acetoxy-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CX)

The compound, m.p. 116° showed elemental analysis compatible with molecular formula C_{30}H_{45}NO_{3}S. The IR spectrum showed bands at 1660 (C=N), 1640 (C=C), 1070 (C=S), 1030 (C=O) and 805 cm^{-1} (N-O). The $^1$H-NMR spectrum of the compound displayed a multiplet at $\delta$ 4.7 ($W = 16$ Hz) for (C3α-H). The methyl protons were observed at $\delta$ 1.2 (C10-CH$_3$), 0.72 (C13-CH$_3$), 0.91 and 0.81. The mass spectrum of the compound (CX) exhibited fragment ion peaks at m/z 455, 439, 425, 386, 379, 365, 266, 252 and lower mass fragment ions. Genesis of some of the important fragment ions is given in Scheme-2. On the basis of above evidences the compound, m.p. 116° was characterized as 3β-acetoxy-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CX).
Reaction of 3β-chloro-6-nitrocholest-5-ene (LIV) with carbon disulphide in triethylamine acetonitrile: 3β-Chloro-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CXL)

3β-Chloro-6-nitrocholest-5-ene (LIV) (2.0 g, 4.45 m mol) in acetonitrile and triethylamine (4.5 g, 44.5 m mol) followed by carbon disulphide (0.91 g, 12 m mol) addition under the similar reaction conditions and usual work up as mentioned earlier afforded the product (CXL) m.p. 131°.
Characterization of the compound, m.p. 131° as 3β-chloro-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CXI)

The compound m.p. 131° was analysed for C_{28}H_{42}NOSCl. The IR spectrum showed bands at 1660 (C=N), 1610 (C=C), 1060 (C=S) 1010 (C-O) and 810 cm\(^{-1}\) (N-O). The \(^1\)H-NMR spectrum of the compound displayed multiplet at \(\delta 3.83\) (\(J_2^1 = 16\) Hz) for (C3α-H). The methyl protons were observed at \(\delta 1.1\) (C1O-CH\(_3\)), 0.70 (C13-CH\(_3\)), 0.90 and 0.80. The mass spectrum of the compound (CXI) gave significant fragment ion peaks at m/z 445/447, 439, 415/417, 409, 395, 379, 326 and lower mass fragment ion peaks. Formation of some of the important fragment ion peaks has been rationalized in Scheme-3. In the light of above discussion the compound, m.p. 131° was characterized as 3β-chloro-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CXI).
The formation of steroidal oximinothiocarboxylic anhydride (CIX - CXI) was explained by the mechanism suggested in Scheme-4.
SCHEME-4

R = H, OAc, Cl
Experimental

Reaction of 6-nitrocholest-5-ene (LV) with carbon disulphide, triethylamine in acetonitrile; 6-Oximinocholest-4-ene-4-thiocarboxylic anhydride (CIX)

To a stirred solution of 6-nitrocholest-5-ene (LV) (2 g, 4.98 m mol) in acetonitrile (15 ml) was added triethylamine (4.5 g, 44.5 m mol) followed by carbon disulphide (0.91, 12 m mol). The mixture was stirred at room temperature for 72 hrs. The progress of reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the residue was taken up in dichloromethane and washed with water, sodium bicarbonate solution (50%) and again with water. The organic layer was dried over anhydrous sodium sulphate. The solvent was evaporated and semi-solid thus obtained was recrystallized from methanol to give cyclized product 6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CIX) (1.25 g, 2.72 m mol), m.p. 110°.

Analysis Found : C, 76.2; H, 9.7; N, 3.2

C_{28}H_{43}NOS requires : C, 76.19; H, 9.75; N, 3.17%. 
IR : \( \nu_{\text{max.}} 1650 \text{ (C=N)}, 1640 \text{ (C=C)}, 1080 \text{ (C=S)}, 1020 \text{ (C-O)}, \) and 815 cm\(^{-1}\) (N-O).

\(^1\)H-NMR : \( \delta 1.20 \text{ (C10-CH}_3\text{)}, 0.68 \text{ (C13-CH}_3\text{)}, 0.90 \text{ and } 0.80 \text{ (other methyl protons)}.

MS : 441 (C\(_{28}\)H\(_{43}\)NOS, absent), 397 (10.00), 386 (9.2), 385 (4.6), 384 (9.2), 382 (4.6), 381 (13.4), 375 (1.15), 374 (4.6), 373 (18.40), 372 (4.6), 371 (75.90), 370 (18.4), 369 (13.8), 368 (4.6), 367 (10.00), 360 (2.3), 359 (3.45), 358 (2.3), 357 (6.9), 356 (4.6), 355 (3.45), 354 (4.6), 345 (4.6), 344(2.3), 343 (3.45), 341 (1.15), 332 (1.15), 331 (2.3), 330 (1.15), 328 (3.45), 327 (1.76), 318 (1.15), 316 (3.45), 315 (0.57), 314 (2.3), 312 (2.3), 303 (1.15), 302 (9.20), 301 (1.15), 300 (2.30), 299 (1.15), 298 (0.57), 289 (0.57), 288 (6.9), 286 (16.1), 285 (2.3), 284 (0.57), 283 (1.15), 276 (0.57), 275 (0.57), 274 (4.6), 273 (6.9), 272 (11.50), 271 (0.57), 270 (2.3), 269 (1.15), 268 (4.6), 264 (0.57), 263 (1.15), 262 (0.57), 261 (0.57), 260 (9.2), 259 (2.3), 258 (2.3), 257 (11.5), 256 (6.9), 255 (4.6), 254 (9.2), 253 (1.15), 252 (1.15), 251 (1.15), 250 (0.57), 249 (0.57), 248 (2.3), 247 (4.6), 246 (4.6), 245 (3.45), 244 (11.5), 243 (4.6), 242 (3.45), 241 (2.3), 240 (2.3), 239 (0.57), 233 (2.3), 232 (9.2), 231 (4.0), 230 (6.9), 229 (6.9), 228 (4.6), 227 (3.45), 226 (0.57), 225 (0.57), 224 (0.57), 223 (0.57), 219 (4.6),
: 125 :

218 (9.2), 217 (4.6), 216 (4.6), 215 (9.2), 212 (2.3), 211 (0.57), 210 (0.57), 209 (0.57), 208 (0.57), 207 (0.57), 206 (2.3), 205 (3.45), 204 (3.45), 203 (0.57), 202 (4.6), 201 (6.9), 200 (4.6), 199 (4.6), 197 (2.3), 196 (2.3), 195 (6.9), 194 (0.57), 193 (2.3), 192 (1.15), 191 (4.6), 190 (8.05), 189 (9.2), 188 (4.6), 187 (1.15), 186 (0.57), 185 (0.57), 184 (1.15), 183 (0.57), 182 (0.57), 181 (1.15), 180 (1.15), 179 (1.15), 178 (0.57), 176 (4.6), 174 (6.9), 173 (2.3), 172 (4.6), 170 (3.45), 169 (0.57), 168 (1.15), 167 (1.15), 166 (0.57), 162 (9.2), 160 (25.30), 159 (11.50), 158 (4.6), 157 (0.57), 156 (1.15), 154 (0.57), 152 (0.57), 151 (6.9), 150 (9.2), 149 (18.4), 148 (29.90), 147 (32.20), 146 (6.9), 145 (29.9), 144 (4.6), 143 (2.3), 142 (1.15), 141 (2.3), 140 (0.57), 137 (18.4), 136 (4.6), 135 (11.5), 134 (2.3), 132 (4.6), 130 (4.6), 124 (11.5), 122 (23.0), 120 (27.6), 118 (27.6), 117 (4.6), 116 (2.3), 114 (0.57), 112 (2.3), 111 (25.30), 110 (4.6), 109 (23.0), 108 (6.9), 107 (23.0), 106 (29.9), 105 (59.8), 104 (2.3), 102 (1.15), 101 (0.57), 100 (0.57), 98 (0.57), 97 (6.9), 96 (2.3), 95 (23.0), 93 (18.4), 92 (0.57), 91 (18.4), 86 (1.15), 85 (0.57), 84 (1.15), 83 (6.9), 82 (2.3), 81 (32.20), 80 (2.3), 79 (23.00), 78 (0.57), 77 (9.2), 71 (18.4), 69 (3.45), 68 (25.30), 67 (18.40), 66 (0.57), 65 (0.57), 58 (0.57), 57 (55.2), 56 (11.5), 55 (48.30), 54 (0.57), 53 (4.6), 52 (0.57), 51 (0.57), 44 (1.15), 43 (100.00), 42 (11.5), 41 (50.6), 40 (50.6).
Reaction of 3β-acetoxy-6-nitrocholest-5-ene (XXXIII) with carbon disulphide, triethylamine, in acetonitrile: 3β-Acetoxy-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CX)

To a stirred solution of 3β-acetoxy-6-nitrocholest-5-ene (XXXIII) (2 g, 4.10 m mol) in acetonitrile (15 ml) was added triethylamine (4.5 g, 44.5 m mol) followed by carbon disulphide (0.91 g, 12 m mol). The mixture was stirred at room temperature for 72 hrs. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the residue was taken up in dichloromethane and washed with water, sodium bicarbonate solution (5%) and again with water. The organic layer was dried over anhydrous sodium sulphate. The solvent was evaporated and semi-solid obtained was recrystallized from methanol to give 3β-acetoxy-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CX) (1.32 q, 2.69 m mol) m.p. 116°.

Analysis Found: C, 72.2; H, 9.0; N, 2.8
C\textsubscript{30}H\textsubscript{45}NO\textsubscript{3}S requires: C, 72.19; H, 9.01; N, 2.80%

IR: \(\nu\) max. 1660 (C=\(\text{N}\)), 1640 (C=\(\text{C}\)), 1070 (C=S), 1030 (C=O) and 805 cm\(^{-1}\) (N-O).

\(\text{\textsuperscript{1}}\text{H}-\text{NMR:}\) \(\delta\) 4.7 (m, \(J_{1,2} = 16\) Hz, C3α-H), 1.2 (C10-CH\(_3\)), 0.72 (C13-CH\(_3\)), 0.91 and 0.81 (other methyl protons).

MS: M\(^+\) 499 (C\(_{30}\)H\(_{45}\)NO\(_3\)S, absent) m/z 455 (2.4), 454 (7.2), 444 (28.8), 442 (3.6), 441 (4.8), 439 (6.1), 428 (2.4), 425 (4.0), 399 (1.2), 386 (4.6), 385 (24.0), 384 (76.80),
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383 (1.2), 382 (1.2), 379 (0.60), 371 (1.2), 370 (7.2), 369 (26.4), 367 (2.4), 365 (9.6), 357 (3.6), 351 (1.2), 301 (1.2), 292 (1.2), 291 (1.2), 289 (2.4), 272 (1.2), 271 (9.6), 266 (1.2), 264 (1.2), 262 (0.60), 261 (0.60), 252 (1.20), 247 (2.4), 245 (3.6), 244 (4.8), 243 (3.6), 242 (1.2), 237 (3.6), 231 (4.8), 230 (6.0), 229 (24.00), 228 (0.60), 227 (0.60), 217 (1.2), 216 (1.2), 215 (3.6), 214 (0.60), 213 (2.5), 212 (1.2), 211 (12.0), 205 (0.60), 203 (0.60), 201 (2.4), 189 (0.60), 188 (0.60), 187 (1.2), 186 (1.2), 183 (1.2), 182 (0.60), 181 (9.6), 179 (0.60), 177 (2.4), 176 (2.4), 175 (4.8), 174 (1.2), 173 (0.60), 171 (1.2), 167 (0.60), 166 (2.4), 161 (4.8), 160 (2.4), 159 (2.4), 158 (2.4), 157 (1.2), 156 (0.60), 155 (0.60), 153 (1.2), 152 (2.4), 150 (3.6), 149 (16.80), 148 (1.2), 147 (4.8), 146 (0.60), 145 (4.8), 144 (1.2), 143 (2.4), 141 (1.2), 140 (0.60), 138 (0.60), 136 (7.2), 134 (4.8), 133 (7.2), 131 (4.8), 129 (0.60), 123 (12.00), 122 (19.2), 121 (36.00), 120 (7.2), 119 (12.00), 118 (12.00), 117 (2.4), 111 (4.8), 109 (29.2), 108 (19.2), 107 (38.4), 106 (4.8), 105 (24.00), 97 (2.4), 96 (2.4), 95 (38.40), 94 (19.2), 93 (24.00), 92 (1.2), 91 (12.00), 85 (1.2), 84 (1.2), 83 (7.2), 82 (2.4), 81 (24.00), 80 (4.8), 79 (19.2), 78 (1.2), 77 (4.8), 71 (9.6), 70 (2.4), 69 (19.20), 68 (9.6), 67 (16.8), 66 (1.2), 57 (28.8), 56 (4.8), 55 (29.2), 54 (1.2), 53 (2.4), 51 (1.2), 45 (2.4), 44 (2.4), 43 (100.00), 42 (2.4), 41 (28.8).
Reaction of 3β-chloro-6-nitrocholest-5-ene (LIV) with carbon disulphide, triethylamine in acetonitrile: 3β-Chloro-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CXI)

To a stirred solution of 3β-chloro-6-nitrocholest-5-ene (LIV) (2 g, 4.45 m mol) in acetonitrile (15 ml) was added triethylamine (4.5 g, 44.5 m mol) followed by carbon disulphide addition (0.91 g, 12 m mol). The reaction mixture was kept under similar reaction conditions as described earlier. The reaction mixture after usual workup and crystallization from methanol afforded 3β-chloro-6-oximinocholest-4-ene-4-thiocarboxylic anhydride (CXI) (1.28 g, 2.41 m mol), m.p. 131°.

Analysis Found: C, 70.6; H, 8.8; N, 2.9

C_{28}H_{42}NOSCl requires: C, 70.64; H, 8.83; N, 2.94%.

IR: ν_{max.} 1660 (C=N), 1610 (C=C), 1060 (C=S), 1010 (C-O) and 810 cm\(^{-1}\) (N-O).

\( ^{1}H\)-NMR:  δ 3.83 (m, W\(^{1/2}\) = 16 Hz; C3α-H), 1.1 (C10-CH\(_{3}\)), 0.70 (C13-CH\(_{3}\)), 0.90 and 0.80 (other methyl protons).

MS: M\(^{+}\), 475/477 (C\(_{28}\)H\(_{42}\)NOSCl, absent), 439(5.0), 417(4.8), 415 (14.7), 409(4.8), 401/403(19.2/6.3), 402(19.2), 395(2.4), 388 (4.8), 387(1.2), 386(7.2), 379(4.6), 371(12.00), 370(45.60), 369(28.80), 368 (28.80), 367(100.00), 366 (4.8), 365 (2.4), 354 (2.4), 352 (2.4), 327 (3.6), 326 (2.4), 323 (9.6),
300 (2.4), 288 (4.8), 287 (6.0), 272 (1.2), 262 (1.2), 260 (2.4), 257 (2.4), 255 (4.8), 254 (16.8), 252 (1.2), 248 (1.2), 247 (4.8), 246 (0.60), 244 (1.2), 240 (1.2), 237 (1.2), 232 (1.2), 230 (1.2), 218 (1.2), 215 (2.40), 213 (3.6), 207 (3.6), 204 (2.4), 201 (2.4), 199 (2.4), 192 (1.2), 188 (1.2), 187 (1.2), 186 (1.2), 164 (2.4), 162 (2.4), 161 (4.8), 160 (2.4), 159 (12.00), 157 (1.2), 151 (2.4), 149 (3.6), 146 (4.8), 145 (6.0), 136 (2.4), 134 (3.6), 132 (7.2), 131 (4.8), 127 (43.2), 126 (19.20), 123 (2.4), 120 (2.4), 111 (1.2), 109 (1.2), 106 (3.6), 104 (3.6), 97 (2.40), 94 (7.2), 92 (1.2), 82 (2.4), 80 (3.60), 71 (1.2), 68 (1.2), 61 (24.00), 60 (3.60), 59 (3.60), 57 (4.8), 55 (2.4), 45 (2.40), 44 (3.60), 43 (4.80).
References


Part Two

B ~ Syntheses of Steroidal Oxathioline Thiones
B - SYNTHESSES OF STEROIDAL OXATHIOLANE THIONES

Epoxide ring opening reactions have been reported at large in the recent past\textsuperscript{1-4}. The epoxide ring is a very sensitive and opens, generally under mild conditions when it comes in contact with acids or bases\textsuperscript{5-8}. A number of papers dealing with the reactions of epoxides with a variety of reagents have appeared where anionic and cationic cleavages of epoxide ring followed by some novel rearrangements in certain cases have been reported.

James and Shoppee\textsuperscript{9} studied the bromination of 3\textbeta-acetoxy-5, 6\alpha-epoxy-5\alpha-cholestane (I) by using 1 mol bromine in acetic acid under varying conditions and obtained only one product 3\textbeta-acetoxy-5-bromo-6\beta-hydroxy-5\alpha-cholestane (Ia) which gave 3\textbeta-acetoxy-5-bromo-5\alpha-cholestan-6-one (II) on chromic acid oxidation.
Fieser and Rajagopalan\textsuperscript{10} reported that the reaction of cholesterol-\(\alpha\)-oxide (III) with N-bromosuccinimide afforded 3\(\beta\),5-dihydroxy-5\(\alpha\)-cholestan-6-one (IV) and 3\(\beta\)-hydroxy-7\(\alpha\)-bromocholest-4-en-6-one (V).
Shaw and Stevenson\textsuperscript{11} discovered a simple method for the preparation of 4-bromocholest-4-en-3-one (VII) by the treatment of 4\textbeta,5\textepsilon-epoxy-5\textbeta-cholestan-3-one (VI) with hydrobromic acid.
Shoppee et al.\textsuperscript{12} reported the halogenation of 5,6\(\beta\)-epoxy-5\(\beta\)-cholestanate (VIII) in presence of hydrogen chloride in chloroform at 15° to afford 5-chloro-5\(\alpha\)-cholestan-6\(\beta\)-ol (IX) which was oxidised by chromium trioxide - acetic acid at 15° to 5-chloro-5\(\alpha\)-cholestan-6-one (X).

Djerassi et al.\textsuperscript{13} studied the reaction of 3-keto-1,2-epoxy-5\(\alpha\)-cholestanate (XI) with hydrazine hydrate and sodium hydroxide and obtained \(\Delta^2\)-cholesten-1\(\alpha\)-ol (XII). Wharton and Bohlen\textsuperscript{14} also reported the hydrazine hydrate reduction of (VI) into \(\Delta^3\)-cholesten-5\(\beta\)-ol (XIII).
Lehmann et al.\textsuperscript{15} reported that the epoxide (XIV), when irradiated indioxane, gave diketone (XV). The epoxide (XVI) on reaction with pyridine and hydrogen chloride in chloroform afforded (XVII) as product\textsuperscript{16}.
Collins\textsuperscript{17} studied the rearrangement of 4\(\alpha\),5-epoxy-5\(\alpha\)-cholestan-3-one (XVI) with BF\(_3\)-etherate and reported the formation of 5\(\beta\)-\(\alpha\)-norcholestan-3-one (XVII).

Kirk\textsuperscript{18} reported the BF\(_3\)-etherate catalysed rearrangement of 3\(\beta\)-acetoxy-5,6\(\alpha\)-epoxy-6\(\beta\)-methyl steroid (LXIX) which gave 3\(\beta\)-acetoxy-5\(\beta\)-methyl-A-homo-B-nor-4\(\alpha\)-ketone (XX). Transformation of 2\(\alpha\),3\(\alpha\)-oxido-3\(\beta\)-acetoxy-5\(\alpha\)-cholestan (XXI) into (XXII) was also reported\textsuperscript{19}.
Heusler et al.\textsuperscript{20} studied the reaction of 3-oxo-4\textalpha,5-oxido-17\beta-hydroxy-5\alpha-androstane (XXIII) with propionic acid and sulphuric acid and obtained 4-hydroxy-17\textbeta-propionyl testosterone (XXIV).
Fieser reported an exhaustive dichromate oxidation of cholesterol-α-oxide (III) in presence of acetic acid but only 16% yield of hydroxydiketone (XXV) was recovered while with cholesterol-β-oxide (XXVI) 90% yield of (XXV) was obtained.

Knox et al. studied the reaction of 6α,7α-oxido-17α-ethyltestosterone (XXVII) with hydrochloric acid and acetic acid and reported the formation of (XXVIII) as product while the reaction of 5α,6α-epoxide (XXIX) with formic acid gave 3-ketone (XXX).
Batres et al. reported the reaction of 5α,6α-oxido-3-cyclo-ethylene dioxyandrostane-17β-ol (XXXI) with ethylene glycol and piperidine and obtained (XXXIIa) as a product which on treatment with acetone-water in presence of p-TsOH gave the ketone (XXXIIb).
Sondheimer et al.\textsuperscript{25} studied the reaction of 3-ethylene dioxy-5α,6α-oxidopregnan-20-one-17α,21-diol-21-acetate (XXXIII) with perchloric acid and allopregnane-3,20-dione-5α,6β,17α,21-tetrol-21-monoacetate (XXXIV) was obtained as a product.

![Diagram of XXXIII and XXXIV](image)

Ellis et al.\textsuperscript{26} reported the reaction of 3β-acetoxy-5,6α-epoxy-6β-methyl-5α-androstan-17-one (XXXV) with hydroiodic acid (under anhydrous conditions) to obtain 3β-acetoxy-5,6β-dihydroxy-6α-methyl-5α-androstan-17-one (XXXVI) as a product.

![Diagram of XXXV and XXXVI](image)
Kirk et al.\textsuperscript{27} reported the reaction of 6\(\beta\),7\(\beta\)-epoxide (XXXVII) with lithium aluminium hydride and tetrahydrofuran which afforded triol (XXXVIII).

\[ \text{XXXVII} \rightarrow \text{XXXVIII} \]

Hallsworth and Henbest\textsuperscript{28} reported the effect of a hydroxyl group on metal reduction of vicinal epoxides and obtained different products (XXXIX, XL, XLII, XLIII, XLV) with 5\(\beta\),6\(\beta\)-epoxycholestane (XXVI), 6\(\beta\),7\(\beta\)-epoxycholestane-3\(\beta\)-ol (XLI) and 3\(\beta\)-methoxy-1\(\beta\),2\(\beta\)-epoxide (XLIV).

\[ \text{XXVI} \rightarrow \text{XXXIX} + \text{XL} \]
Bowers et al.\textsuperscript{29} reported the formation of cyanosteroids (XLVII) and (XLVIII) when 3\(\beta\)-acetoxy-5\(\alpha\),6\(\alpha\)-epoxide (XLVI) was treated with potassium cyanide at 150\(^\circ\)C.
Blunt et al.\textsuperscript{30} reported the reaction of BF\textsubscript{3}–etherate with 5,6\(\alpha\)-epoxy-5\(\alpha\)-cholestan (XLIX) and obtained rearranged product (L).

Blackett et al.\textsuperscript{31} studied the reaction of 4\(\alpha\),5\(\alpha\) (LI) and 5\(\beta\),6\(\beta\) (VIII) epoxycholestanes with BF\textsubscript{3}–etherate in benzene and obtained rearranged products, cholestan–4\(\alpha\)-ol (LII) and 6\(\alpha\)-ol (LIII) respectively.
Cattel et al.\textsuperscript{32} obtained 13(17)-baccharen-3β-ol (LV) from 3β,4β-epoxyshionane (LIV) in MeNO\textsubscript{2} by the treatment of BF\textsubscript{3}-Et\textsubscript{2}O. The diepoxide (LVI) when treated\textsuperscript{33} with BF\textsubscript{3}-Et\textsubscript{2}O in benzene for 10 minutes at ambient temperature gave compound (LVII) in 66% yield.
The reactions of 5,6α-oxido-5α-cholestan (LI) and its 3β-substituted derivatives (I), (III) and (LXIV) with 1-phenyl-1H-tetrazole-5-thiol in the presence of lithium bromide and dimethyl formamide provided (LVIII–LXI) as the products respectively.
Taguchi and Suhara\textsuperscript{35} reported the reactions of episulphides (LXII) and (LXV) with malononitrile and diethyl malonate and obtained (LXIII)\textsuperscript{=} (LXIV) and (LXVI) as the products respectively.

\begin{align*}
\text{CH}_3 \quad \text{CH} - \text{CH}_2 + \text{NC}-\text{CH}_2-\text{CN} & \rightarrow \quad \text{CH}_3 \quad \text{CH} - \text{CH}_2 \quad \text{NH}\quad \text{CN} \\
\text{(LXII)} & \text{(LXIII)} \quad \text{NH}_2 \\
\text{H}_3\text{C} \quad \text{S} \quad \text{C} - \text{CH}_2 + \text{CH}_2\text{(COOC}_2\text{H}_5)_2 & \rightarrow \quad \text{H}_3\text{C} \quad \text{S} \quad \text{C} - \text{CH}_2 \quad \text{COOC}_2\text{H}_5 \\
\text{(LXV)} & \text{(LXVI)}
\end{align*}

Taguchi and coworkers\textsuperscript{36} also carried out the reaction of episulphide (LXVII) with carbon disulphide in the presence of triethylamine and obtained 4,4-dimethyl-1,3-dithiolane-2-thione (LXVIII) as the product.

\begin{align*}
\text{H}_3\text{C} \quad \text{C} \quad \text{S} \quad \text{CH}_2 + \text{CS}_2 & \quad \text{Et}_3\text{N} \quad \rightarrow \quad \text{CH}_3 \quad \text{S} \quad \text{S} \quad \text{C} - \text{CH}_2 \\
\text{(LXVII)} & \text{(LXVIII)}
\end{align*}
Discussion

Five membered heterocyclic compounds have been obtained by the reaction of thiiranes with ethyl cyanoacetate, malonitrile, acetonitrile, diethylmalonate, ethyl acetacetate and carbondisulphide but no significant work has been done with the steroidal compounds. Herein, the method is extended for the synthesis of [6α,5-d]-1',3'-oxathiolane-2'-thione derivatives (LXIX - LXXII) by the reaction of steroidal epoxides (LI), (III), (I) and (LXIV) with carbon disulphide at room temperature using triethylamine as a catalyst.

The reaction of 5,6α-epoxy-5α-cholestan (LI), its 3β-hydroxy (III), 3β-acetoxy (I) and 3β-chloro (LXIV) analogues with carbon disulphide in triethylamine furnished 5α-cholestano [6α,5-d]-1',3'-oxathiolane-2'-thione (LXIX), its 3β-hydroxy (LXX), 3β-acetoxy (LXXI) and 3β-chloro (LXXII) analogues, respectively.
Reaction of 5,6α-epoxy-5α-cholestane (LI) with carbon disulphide in triethylamine: 5α-Cholestan-6α,5-d-l',3'-oxathiolane-2'-thione (LXIX)

To a stirred solution of steroidal epoxide (LI) in triethylamine was added a solution of carbon disulphide in triethylamine and the reaction mixture was stirred for 76 hrs. The progress of the reaction was monitored by TLC and after the completion of the reaction, the solvent was completely removed under reduced pressure and the residue was worked up in ether and the ethereal solution was washed with water and dried over anhydrous sodium.
sulphate. Evaporation of the solvent gave an oily residue which was recrystallized from acetone to give a solid compound, m.p. 87°.

Characterization of the compound, m.p. 87° as 5α-cholestano[6α,5-d]-1',3'-oxathioline-2'-thione (LXIX)

The elemental analysis of the compound, m.p. 87° corresponded to the molecular formula C_{28}H_{46}O_{2}S_{2}. The IR spectrum of the compound exhibited bands at 1070 (C=S) and 1045 cm⁻¹ (oxathioline ring). The ¹H-NMR spectrum of the compound displayed a double doublet at δ 3.9 which was assigned to C6β-H, J_{aa} = 7 Hz; J_{ae} = 2 Hz. Methyl protons were observed at 61.25 (ClO-CH₃), 0.75 (Cl₃-CH₃), 0.95 and 0.85 (other methyl protons). On the basis of above evidences the compound, m.p. 87° was characterized as 5α-cholestano[6α,5-d]-1',3'-oxathioline-2'-thione (LXIX).

The structure of the compound (LXIX) was further supported by its mass spectral study. The mass spectrum of the compound (LXIX) gave significant fragment ions peaks at m/z 402, 386, 370, 273, 257 and 242 alongwith lower mass fragment ions. The tentative pathways for the formation of some of the fragment ion peaks are given in Scheme-1.
Reaction of 3\(\beta\)-hydroxy-5,6\(\alpha\)-epoxy-5\(\alpha\)-cholestane (III) with carbon disulphide in triethylamine : 3\(\beta\)-Hydroxy-5\(\alpha\)-cholestan [6\(\alpha\),5-\(d\)]-1',3'-oxathiolane-2'-thione (LXX)

3\(\beta\)-Hydroxy-5,6\(\alpha\)-epoxy-5\(\alpha\)-cholestan (II) was dissolved in triethylamine and carbon disulphide in triethylamine was added under stirring. The reaction mixture was stirred for 76 hrs. at room temperature. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was worked up as described earlier. Evaporation of the solvent gave semi-solid residue which was recrystallized from acetone to afford a product, m.p. 132\(^\circ\).
Characterization of the compound, m.p. 132° as 3β-hydroxy-5α-cholestanol[6α,5-d]-1',3'-oxathiolane-2'-thione (LXX)

The compound, m.p. 132° showed elemental analysis, compatible with molecular formula C_{28}H_{46}O_{2}S_{2}. The IR spectrum of the compound showed absorption bands at 3400 (OH), 1060 (C=S) and 1040 cm^{-1} (oxathiolane ring). The ^{1}H-NMR spectrum of the compound displayed a multiplet at δ 4.5 which was assigned to (C3α-H; W_{1/2} = 16 Hz) and a double doublet at δ 3.85 (J_{aa} = 8 Hz; J_{ae} = 3 Hz, axial) was observed for (C6β-H). The other signals were observed at δ 1.23 (C10-CH_{3}), 0.75 (C13-CH_{3}), 0.90 and 0.80. Thus on the basis of elemental analysis and spectral data the compound, m.p. 132° was characterized as 3β-hydroxy-5α-cholestanol[6α,5-d]-1',3'-oxathiolane-2'-thione (LXX). The mass spectrum of the compound (LXX) exhibited fragment ion peaks at m/z 418, 402, 386, 371, 289, 274, 273, 258 and lower mass fragment ions.
Formation of some of the fragment ions are rationalized in Scheme-2.

**SCHEME-2**

![Scheme-2 Diagram](image)

Reaction of 3β-acetoxy-5,6α-epoxy-5α-cholestanol (I) with carbon disulphide and triethylamine: 3β-Acetoxy-5α-cholestanol[6α,5-δ]-1',3'-oxathiolane-2'-thione (LXXI)

3β-Acetoxy-5,6α-epoxy-5α-cholestanol (I) in triethylamine was stirred at room temperature with carbon disulphide and triethylamine at room temperature for 76 hrs. under the conditions as described earlier. A compound, m.p. 181° was obtained after usual work up and crystallization from acetone.
Characterization of the compound, m.p. 181° as 3β-acetoxy-5α-cholestano[6α,5-d]-1',3'-oxathiolane-2'-thione (LXXI)

The compound, m.p. 181° was analysed for C_{30}H_{48}O_{3}S_{2}. The IR spectrum of the compound showed bands at 1735 (CH^2COO^-), 1070 (C=S) and 1040 cm^-1 for oxathiolane ring. The $^1$H-NMR spectrum of the compound displayed a multiplet at $\delta$ 4.5 ($\omega^2=18$Hz) and was assigned to (C3α-H) and a double doublet at $\delta$ 3.8 ($J_{aa}=6$ Hz, $J_{ae}=3$ Hz, axial) was observed for (C6β-H). The acetate methyl protons were observed at $\delta$ 2.0 as a singlet. The other signals were at $\delta$1.23 (ClO-CH_3), 0.70 (Cl3-CH_3), 0.90 and 0.80. The mass spectrum of the compound (LXXI) showed the prominent fragment ion peaks at m/z 460, 444, 429, 428, 384, 369, 368, 271, 255, 240 and lower fragment ion peaks. Formation of some of the fragments has been shown in Scheme-3. Thus on the basis of above discussion the compound, m.p. 181° was characterized as 3β-acetoxy-5α-cholestano[6α,5-d]-1',3'-oxathiolane-2'-thione (LXXI).
Reaction of 3β-chloro-5,6α-epoxy-5α-cholestan (LXIV) with carbon disulphide in triethylamine : 3β-Chloro-5α-cholestano [6α,5-d]-1',3'-oxathiolane-2'-thione (LXXII)

To the stirred solution of epoxide (LXIV) in triethylamine was added a solution of carbon disulphide in triethylamine and the reaction mixture was further stirred for 76 hrs. After the completion of the reaction, the reaction mixture was worked up as described earlier and provided a compound, m.p. 163°.
Characterization of the compound, m.p. 163° as 3β-chloro-5α-cholestano[6α,5-d]-1',3'-oxathiolane-2'-thione (LXXII)

The compound, m.p. 163° showed elemental analysis compatible with molecular formula C_{28}H_{45}OS_{2}Cl (positive Beilstein test). The IR spectrum of the compound showed bands at 1060 (C=S), 1035 (oxathiolane ring) and 750 cm^{-1} (C-Cl). The ^1H-NMR spectrum of the compound showed multiplet at δ 4.6 which was assigned to C3α-H (W_{1/2} = 14 Hz) and a double doublet at δ 3.9 (J_{aa} = 6 Hz, J_{ae} = 3 Hz, axial) was observed for (C6β-H). Angular and side chain methyl protons were observed at δ 1.25 (C10-CH_{3}), 0.75 (C13-CH_{3}), 0.96 and 0.86. The mass spectrum of the compound, m.p. 163° gave prominent fragment ion peaks at m/z 436/438, 420/422, 415/417, 404/406, 368, 255, 240 and lower mass fragment
ions. Formation of some of the fragment ions has been shown in Scheme-4. Thus on the basis of above discussion the compound, m.p. 163° was characterized as 3β-chloro-5α-cholestan-[6α,5-d]-1',3'-oxathiolane-2'-thione (LXXII).

Formation of [6α,5-d]-1',3'-oxathiolane-2'-thiones was explained by the mechanism suggested as below:
MECHANISM OF THE REACTION

$$\text{Et}_3\text{N}: + \text{CS}_2 \rightarrow \text{Et}_3\text{N} - \text{C} - \text{S}$$

$$R = \text{H, OH, OAc, Cl}$$
Experimental

5,6α-Epoxv-5α-cholestane (I):  
Cholest-5-ene (6.0 g) in chloroform (40 ml) was treated with a solution of perbenzoic acid (1.1 mole equivalent) in chloroform and kept at -8°C for 20 hrs. The mixture was then washed with ice cold water, sodium bicarbonate solution (5%), sodium thiosulphate solution (5%) and water. Evaporation of the solvent yielded 5,6α-epoxy-5α-cholestane (I) as an oil which was crystallized from acetone as needles (4.3 g) m.p. 76°C (reported, m.p. 76°C).

3β-Hydroxy-5,6α-epoxy-5α-cholestane (III):  
Cholesterol (11.0 g) in chloroform (100 ml) was treated with a solution of perbenzoic acid (1.1 mole equivalent) in chloroform and kept at -8°C for 20 hrs. The progress of the reaction was monitored by TLC. After the completion of the reaction the mixture was washed with ice cold water, sodium bicarbonate solution (5%), sodium thiosulphate solution (5%) and water. Evaporation of the solvent gave an oil which was crystallized from acetone to give 3β-hydroxy-5,6α-epoxy-5α-cholestane (III) (8.1 g), m.p. 142°C (reported, m.p. 142.5°C).
3β-Acetoxy-5,6α-epoxy-5α-cholestane (I):

3β-Acetoxycholesterol-5-ene (10 g) in chloroform (100 ml) was treated with a solution of perbenzoic acid (1.1 mole equivalent) in chloroform and kept at -8° for 20 hrs. The reaction mixture was then washed successively with ice-cold water sodium bicarbonate solution (5%), sodium thiosulphate solution (5%) and water. Evaporation of the solvent gave a solid material which was recrystallized from acetone to give 3β-acetoxy-5,6α-epoxy-5α-cholestane (I), (7.0 g), m.p. 97° (reported\(^8\), m.p. 97°).

3β-Chloro-5,6α-epoxy-5α-cholestane (LXXV):

3β-Chlorocholesterol-5-ene (11.0 g) in chloroform (100 ml) was treated with a solution of perbenzoic acid (1.1 mole equivalent) and kept at -8° for 20 hrs. The progress of the reaction was monitored by TLC. After the completion of the reaction, the mixture was washed successively with ice-cold water sodium bicarbonate solution (5%), sodium thiosulphate solution (5%) and again with water. Evaporation of the solvent yielded an oil which was recrystallized from acetone to give 3β-chloro-5,6α-epoxy-5α-cholestane (LXXV) as needles (8.1 g), m.p. 89° (reported\(^8\), m.p. 89.5–90.5°).
Reaction of 5,6α-epoxy-5α-cholestan (LI) with carbon disulphide and triethylamine: 5α-Cholestan\[6α,5-d\]-1',3'-oxathiolane-2'-thione (IXIX)

To a stirred solution of 5,6α-epoxy-5α-cholestan (LI) (2.0 g, 5.18 mmol) in triethylamine (5 ml) was added a solution of carbon disulphide (1.25 ml, 25 mmol) in triethylamine (1 ml) at room temperature. Progress of the reaction was monitored by TLC. After the completion of the reaction, the solvent was removed under reduced pressure and the residue thus obtained was taken in ether. The ethereal solution was washed with water several times and dried over anhydrous sodium sulphate. Evaporation of the solvent gave the semi-solid which was recrystallized from acetone to afford the product (IXIX) (1.6 g, 4 mmol), m.p. 87-88°.

Analysis Found: C, 72.0; H, 9.9

C_{28}H_{46}OS_{2} requires: C, 72.72; H, 9.95%.

IR: $\gamma_{\max}$ 1070 (C=S) and 1045 cm^{-1} (oxathiolane ring).

$^1$H-NMR: δ 3.9 (dd, 1H, $J_{aa} = 7$ Hz, $J_{ae} = 2$ Hz, axial, C6β-H), 1.25 (C10-CH$_3$), 0.75 (C13-CH$_3$), 0.95 and 0.85 (other methyl protons).

MS: 462 (C$_{28}$H$_{46}$O$_{2}$, absent), 402 (16.31), 387 (23.30), 386 (16.31), 370 (15.83; C$_{27}$H$_{46}$), 369 (25.63), 368 (93.20), 367 (1.67), 366 (1.63), 353 (4.66), 352 (16.31), 274 (1.63), 273 (2.66), 270 (4.66), 261 (6.99), 260 (16.31), 259 (11.65),
258 (11.65), 257 (32.62), 256 (2.33), 255 (11.65), 244 (1.66), 242 (9.32), 241 (3.96), 240 (2.3), 229 (2.3), 228 (2.33), 227 (1.63), 215 (1.63), 214 (2.33), 213 (11.65), 212 (1.63), 211 (1.63), 207 (1.66), 206 (2.33), 205 (2.33), 201 (2.33), 199 (2.33), 198 (3.96), 197 (2.33), 193 (1.63), 191 (1.63), 187 (1.63), 186 (1.63), 185 (2.33), 183 (1.63), 176 (1.63), 175 (1.63), 173 (4.66), 172 (1.63), 171 (2.33), 169 (1.63), 165 (1.63), 164 (6.99), 163 (6.9), 161 (2.33), 160 (11.65), 159 (11.65), 158 (16.31), 157 (6.99), 156 (1.63), 155 (1.63), 151 (1.63), 149 (9.32), 148 (9.32), 147 (34.95), 146 (11.65), 145 (30.29), 144 (11.65), 143 (13.98), 142 (2.33), 141 (2.33), 137 (2.33), 136 (1.63), 135 (11.65), 134 (6.99), 133 (16.31), 132 (4.66), 131 (16.31), 129 (3.69), 127 (9.32), 125 (1.66), 122 (4.66), 121 (2.33), 120 (16.31), 119 (16.31), 118 (13.98), 117 (9.32), 116 (1.63), 115 (1.63), 110 (2.33), 109 (11.65), 108 (9.32), 107 (9.32), 106 (23.30), 105 (32.62), 104 (1.63), 103 (1.63), 97 (6.99), 96 (1.63), 95 (32.62), 93 (23.30), 91 (6.99), 90 (23.30), 85 (2.33), 83 (11.65), 82 (4.66), 80 (30.29), 79 (1.66), 78 (2.33), 77 (9.32), 71 (16.31), 70 (1.66), 69 (23.30), 68 (1.63), 67 (25.63), 65 (1.65), 61 (1.66), 57 (37.28), 56 (4.66), 55 (34.95), 53 (2.33), 51 (1.63), 45 (1.66), 44 (1.63), 42 (1.63), 41 (100.00).
Reaction of 3β-hydroxy-5,6α-epoxy-5α-cholestane (III) with carbon disulphide and triethylamine: 3β-Hydroxy-5α-cholestano-
[6α,5-d]-1',3'-oxathiolane-2'-thione (LXX)

To a stirred solution of 3β-hydroxy-5,6α-epoxy-5α-cholestane (III) (2.0 g, 5 m mol) in triethylamine (5 ml) was added a solution of carbon disulphide (1.25 ml, 25 m mol) in triethylamine (1 ml), under the similar reaction conditions described in the previous experiment. After usual work up of the reaction mixture and crystallization of the oily residue, obtained after the evaporation of the solvent, afforded 3β-hydroxy-5α-cholestano-
[6α,5-d]-1',3'-oxathiolane-2'-thione (LXX) (1.5 g, 4.4 m mol), m.p. 132°.

Analysis Found: C, 71.0; H, 9.6
C28H46O2S2 requires: C, 70.37; H, 9.62%

IR: $\gamma_{\text{max}}$ 3400 (OH), 1060 (C=S) and 1040 cm$^{-1}$ (oxathiolane ring).

$^1$H-NMR: $\delta$ 4.5 (m, 1H, $W_2^I$ = 16 Hz, axial, C3α-H), 3.85 (dd, 1H, $J_{aa} = 8$ Hz, $J_{ae} = 3$ Hz, axial, C6β-H), 1.23 (C10-CH$_3$), 0.75 (C13-CH$_3$), 0.90 and 0.80 (other methyl protons).

MS: 478 (C$_{28}$H$_{46}$O$_2$S$_2$, absent), 418 (12.00), 416 (14.80), 402 (16.80), 386 (2.4; C$_{27}$H$_{46}$O), 371 (14.40), 370 (4.8), 369 (33.60), 368 (100.00), 354 (4.8), 353 (16.80), 325 (1.2), 289 (11.40), 274 (36.0), 273 (7.20), 260 (3.6), 259 (18.00), 258 (0.61), 257 (4.8), 256 (4.8), 255 (12.00), 248 (3.60), 247 (16.80), 246 (1.20), 245 (1.20), 240 (2.40),
Reaction of 3β-acetoxy-5,6α-epoxy-5α-cholestané (I) with carbon disulphide and triethylamine: 3β-Acetoxy-5α-cholestanó-[6α,5-δ]-1',3'-oxathiolane-2'-thione (LXXI)

To a stirred solution of 3β-acetoxy-5,6α-epoxy-5α-cholestané (I) (2.0 g, 4.50 mmol) in triethylamine (5 ml) was added a solution of carbon disulphide (1.25 ml, 25 m mol) in triethylamine (1 ml), under the similar reaction conditions described earlier. After
usual work up of the reaction mixture and crystallization of
the semi-solid thus obtained from acetone afforded 3β-acetoxy-
5α-cholestan-6α,5-d-1,3'-oxathiolane-2'-thione (LXXI)
(1.3 g, 3 m mol), m.p. 181°.

Analysis Found : C, 69.2; H, 9.3
C₃₀H₄₈O₃S₂ requires : C, 69.23; H, 9.23%.

IR : $\nu_{\text{max}}$ 1735 (CH₂COO⁻), 1070 (C=S) and 1040 cm⁻¹
(oxathiolane ring).

$^1$H-NMR : δ 4.5 (m, 1H, $J_a = 18$ Hz; axial, C3α-H), 3.8 (dd, 1H,
$J_{aa} = 6$ Hz, $J_{ae} = 3$ Hz, axial, C6β-H), 2.0 (s, 3H,
CH₃COO⁻), 1.23 (C10-CH₃), 0.70 (C13-CH₃), 0.90 and
0.80 (other methyl protons).

MS : 520 (C₃₀H₄₈O₃S₂⁻ absent), 460 (38.80), 444 (2.4),
429 (12.00), 428 (10.80), 427 (6.0), 420 (2.4), 405 (2.4),
404 (9.6), 403 (9.6), 402 (24.00), 390 (1.2), 389 (1.2),
388 (2.4), 387 (12.00), 385 (9.6), 384 (24.00), 370 (2.4),
369 (9.60), 368 (16.80), 367 (38.40), 366 (36.60), 365
(1.2), 357 (1.2), 356 (4.8), 355 (1.2), 354 (1.2), 353 (2.4),
352 (4.8), 351 (12.00), 350 (1.2), 292 (1.2), 291 (3.6),
289 (4.8), 282 (1.2), 280 (2.4), 279 (1.2), 278 (0.68), 277
(0.61), 276 (1.2), 275 (2.4), 274 (2.4), 272 (4.8), 271
(24.00), 270 (7.2), 266 (2.4), 265 (12.00), 264 (9.6), 262
(9.6), 261 (33.60), 260 (12.00), 259 (1.2), 258 (1.2),
256 (0.61), 255 (9.60), 254 (3.60), 253 (4.8), 252 (16.80), 251 (3.60), 250 (14.40), 249 (48.00), 248 (55.20), 246 (45.60), 245 (4.80), 244 (4.80), 243 (3.60), 241 (2.40), 240 (4.80), 239 (9.60), 238 (4.80), 237 (2.40), 236 (1.20), 235 (7.20), 234 (9.60), 232 (14.40), 231 (9.60), 230 (4.80), 229 (7.2), 228 (12.00), 227 (7.20), 225 (36.00), 224 (2.4), 214 (9.60), 212 (48.00), 211 (24.00), 210 (48.00), 209 (4.8), 208 (4.8), 207 (2.40), 206 (4.80), 205 (4.80), 200 (9.60), 199 (7.20), 198 (24.00), 197 (14.40), 196 (36.60), 195 (9.60), 194 (9.60), 193 (9.60), 191 (2.4), 190 (4.80), 188 (9.60), 186 (12.00), 185 (9.60), 183 (24.00), 182 (9.60), 180 (16.80), 178 (9.6), 176 (12.00), 174 (24.00), 173 (12.00), 172 (12.00), 171 (16.80), 170 (36.00), 169 (16.80), 168 (31.20), 166 (14.40), 165 (7.20), 164 (14.40), 162 (24.00), 161 (43.20), 160 (24.00), 159 (48.00), 158 (36.00), 157 (74.40), 156 (14.40), 150 (12.00), 149 (14.40), 148 (7.20), 146 (24.00), 145 (24.00), 144 (9.60), 143 (24.00), 142 (7.2), 140 (12.00), 139 (1.20), 138 (1.20), 137 (7.20), 136 (12.00), 135 (14.40), 134 (24.00), 133 (12.00), 132 (26.40), 131 (9.6), 130 (7.2), 129 (14.40), 128 (12.00), 127 (2.40), 126 (1.20), 125 (1.20), 124 (2.40), 123 (21.60), 122 (19.20), 120 (28.80), 119 (26.40), 118 (33.60), 117 (14.40), 116 (7.20), 115 (16.80), 111 (12.00), 110 (38.40), 109 (45.60), 108 (26.40), 107 (52.80), 106 (19.20), 105 (16.80), 104 (57.60), 103 (7.20), 102 (2.40), 98 (2.40), 97 (16.80), 96 (86.40), 95 (26.40), 94 (24.00), 93 (76.80), 92 (16.80), 90 (67.20), 85 (9.60), 84 (12.00), 83 (50.40), 82 (28.80), 81 (100.00), 80 (24.00), 79 (86.40), 78 (16.80),
Reaction of 3β-chloro-5,6α-epoxy-5α-cholestan-6β-ol (LXIV) with carbodisulphide and triethylamine : 3β-Chloro-5α-cholestan-[6α,5-d]-1',3'-oxathiolane-2'-thione (LXXII)

To a stirred solution of 3β-chloro-5,6α-epoxy-5α-cholestan-6β-ol (LXIV) (2.0 g, 4.96 mmol) in triethylamine (5 ml) was added a solution of carbon disulphide (1.25 ml, 25 mmol) in triethylamine (1 ml), under the similar reaction conditions described earlier. The mixture after usual work up and crystallization furnished 3β-chloro-5α-cholestan-[6α,5-d]-1',3'-oxathiolane-2'-thione (LXXII) (1.4 g, 3.1 mmol), m.p. 163°.

Analysis Found : C, 70.0; H, 8.3
C_28H_{45}OS_2Cl requires : C, 70.01; H, 8.25%

IR : \( \nu_{\text{max}} \) 1060 (C=S), 1035 (oxathiolane ring) and 750 cm\(^{-1}\) (C-Cl).

\(^1\)H-NMR : \( \delta \) 4.6 (m, 1H, \( J_{\alpha\beta} = 14 \text{ Hz} \); axial, C3α-H); 3.9 (dd, 1H, \( J_{\alpha\beta} = 6 \text{ Hz}, J_{\alpha\gamma} = 3 \text{ Hz} \); axial, C6β-H), 1.25 (C10-CH\(_3\)), 0.75 (C13-CH\(_3\)), 0.96 and 0.86 (other methyl protons).

MS : 496/498 (C\(_{28}\)H\(_{45}\)OS\(_2\)Cl, absent), 436/438 (14.40/4.80), 420/422 (12.00/3.60), 415/417 (7.2/2.4), 404/406 (11.76/3.80);
C_{27}H_{45}Cl, 368 (14.40), 298 (1.20), 289 (0.61), 287 (1.20); 286 (3.60), 285 (4.80), 284 (4.80), 283 (3.60), 279 (0.61), 275 (0.61), 273 (1.20), 272 (0.61), 269 (1.20), 265 (0.61), 263 (1.20), 255 (9.6), 250 (0.61), 249 (1.20), 248 (1.20), 240 (8.40), 235 (0.61), 233 (0.61), 227 (1.20), 225 (1.20), 221 (0.61), 213 (4.80), 211 (4.80), 209 (0.61), 207 (0.61), 205 (0.61), 199 (0.61), 197 (4.80), 195 (4.80), 193 (8.40), 177 (0.61), 175 (1.20), 173 (4.80), 171 (4.80), 169 (0.61), 168 (3.60), 160 (9.60), 158 (12.00), 157 (14.40), 156 (7.20), 155 (9.60), 154 (1.20), 153 (0.61), 152 (1.20), 151 (2.40), 149 (7.20), 148 (7.20), 147 (14.40), 146 (7.20), 145 (14.40), 142 (7.20), 141 (9.60), 137 (2.40), 135 (12.00), 133 (24.00), 132 (4.80), 131 (29.20), 130 (8.40), 128 (14.40), 127 (3.60), 123 (9.60), 121 (24.00), 120 (12.00), 119 (33.60), 118 (16.80), 117 (57.60), 115 (72.00), 114 (7.20), 113 (12.00), 111 (12.00), 109 (12.00), 107 (24.00), 106 (16.80), 105 (69.60), 104 (7.20), 103 (9.20), 101 (3.60), 100 (4.80), 95 (1.20), 94 (3.60), 90 (2.40), 83 (1.20), 82 (4.80), 80 (4.80), 78 (3.60), 76 (1.20), 71 (7.20), 69 (4.80), 68 (1.20), 67 (7.20), 65 (1.20), 57 (24.00), 56 (2.40), 55 (19.20), 54 (1.20), 53 (2.4), 44 (3.60), 43 (100.00), 42 (9.60), 41 (21.60), 40 (24.00).
References


Part Three

Lead Tetra Acetate
Oxidation of
Steroidal Compounds
Lead tetra acetate (LTA) has drawn the attention of many organic chemists in the recent past because of its versatile nature and many interesting results of its reaction with a variety of organic substrates. Lead tetra acetate not only acts as an oxidant, but its other properties include oxidation of double bond, allylic oxidation, acylation or alkylation, carbonyl formation, double bond migration. Lead tetra acetate can be used to introduce methyl or acetoxy group at suitable activated positions in organic compounds. Here, in this chapter, the reactions of lead tetra acetate with various substrates are discussed.

Lead tetra acetate reacts with 1,2-diols to form carbonyl compounds. The reaction has been formulated as passing through cyclic ester as intermediate.

\[
Pb(OAc)_2 + \text{C}=O + O\equiv \text{C} \rightarrow Pb(OAc)\overset{\text{C}^\equiv \text{O}}{\text{C}=\text{C}} + \text{AcO}^{-} \overset{\text{OAc}}{\text{OAc}} + \text{CH}_3\text{COOH}
\]
Amorosa and coworkers\textsuperscript{14} reported the reaction of lead (IV) acetate with 3\(\beta\)-acetoxy-17\(\beta\)-hydroxy-5\(\alpha\)-pregnane in presence of methanol and benzene to obtain 3\(\beta\)-acetoxy-17-oxo-13,17-seco-5\(\alpha\)-pregnene (II) and 3\(\beta\),13\(\alpha\)-diacetoxy-17-oxo-13,17-seco-5\(\alpha\)-pregnane (III) as the products whereas compound (IV) gave (V).
Caspi, et al.\textsuperscript{15} reported the reaction of (VI) with lead (IV) acetate in presence of methanol and benzene to obtain (VII) and (VIII) as products.

\[ \text{Pb(OAc)}_4, \text{MeOH, C}_6\text{H}_6, \text{r.t., 16 hrs} \]

(VI) → (VII) + (VIII)

Meystre and coworkers\textsuperscript{16} reported the reaction of 3\(\beta\), 11\(\alpha\)-diacetoxy-20\(\beta\)-hydroxy-5\(\alpha\)-pregnane (IX) with lead (IV) acetate and obtained 3\(\beta\), 11\(\alpha\)-diacetoxy-18,20\(\beta\)-oxido-5\(\alpha\)-pregnane (X) as product.
Heusler and coworkers$^{17}$ reported the formation of $3\alpha,11\beta$-diacetoxy-$18,20\beta$-oxido-$5\beta$-pregnane (XII) from $3\alpha,11\beta$-diacetoxy-$20$-hydroxy-$5\beta$-pregnane (XI) while (IX) gave (X) and $3\beta,11\alpha$-diacetoxy-$20\beta$-acetoxo-$5\beta$-pregnane (XIII) as the products.

\[
\begin{align*}
\text{Pb(OAc)}_4, \text{CH}_3\text{-C}_6\text{H}_{11} & \quad 7 \text{ hrs} \\
\text{(XI)} & \rightarrow \text{(XII)} \\
\text{(IX)} & \rightarrow \text{(X) + (XIII)}
\end{align*}
\]
Cainelli and coworkers\textsuperscript{18} reported the reaction of lead (IV) acetate in the presence of cyclohexane with (20S)-3-ethylenedioxy-20-hydroxy-\(\Delta^5\)-pregnene(XIV) and (20S)-3-ethylenedioxy-18,20-oxido-\(\Delta^5\)-pregnene(XV) and 20(S)-3-ethylenedioxy-\(\Delta^5\)-pregnene(XVI) as the products were obtained.

\[
\begin{align*}
\text{Pb(OAc)}_4 & \quad \Delta, 11 \text{ hrs, } C_6H_{12} \\
\text{(XIV)} & \quad \text{(XV)} \\
\end{align*}
\]

Reichstein and Montinel showed the reaction of lead (IV) acetate with 20-oxo-5\(\alpha\)-pregnan-3\(\beta\)-yl-acetate (XVII) in the presence of acetic acid and obtained (XVIII) as the product. \(\alpha\)-Acetoxylated product (XX) was obtained from (XIX)\textsuperscript{6}. 

\[
\begin{align*}
\text{Pb(OAc)}_4 & \quad \Delta, 11 \text{ hrs, } C_6H_{12} \\
\text{(XIV)} & \quad \text{(XV)} \\
\text{(XVI)} & \quad \text{(XVIII)} \\
\end{align*}
\]
Nambara and Fishman reported the formation of 17-oxo-5α, 14β-androstan-3β,16α-dioldiacetate (XXII) with the reaction of lead (IV) acetate with 3β,17-diacetoxy-5α,14β-androst-16-ene (XXI).
Armas et al.\textsuperscript{21} reported the reaction of (XXIIIa–e) with lead (IV) acetate and obtained different products (XXIVa–e) and (XXVa–e).

\[
\begin{array}{ccc}
\text{(XXIII)} & \text{(XXIV)} & \text{(XXV)} \\
R^1 & R^2 & R^1 & R^2 \\
(a) & H_2 & \text{NOH} & (a) & H & (a) & H_2 & \text{NOH} \\
(b) & H_2 & \text{N-NO}_2 & (b) & H & (b) & H_2 & \text{N-NO}_2 \\
(c) & H_2 & \alpha-\text{H}, \beta-\text{NHNO}_2 & (c) & H & (c) & H_2 & \alpha-\text{H}, \beta-\text{NHNO}_2 \\
(d) & \alpha-\text{H}, \beta-\text{OAc} & \alpha-\text{H}, \beta-\text{NHNO}_2 & (d) & \text{OAc} & (d) & \alpha-\text{H}, \beta-\text{OAc} & \alpha-\text{H}, \beta-\text{NHNO}_2 \\
(e) & \text{NNHTS} & H_2 & (e) & H & (e) & H_2 & H_2
\end{array}
\]

Sehgal\textsuperscript{22} reported the formation of 5α-bromo-20-oxo-6β,19-epoxy pregnan-3β-yl acetate (XXVIII) from 3β-acetoxy pregnanone bromohydrin (XXVII) which was obtained from 3β-acetoxy pregnenone (XXVI) with the reaction of HOBr.
Mihailovic et al. studied the reaction of lead (IV) acetate with 3-oxo-4β,5-oxido-5β-cholestane (XXIX) and obtained 2β-acetoxy-3-oxo-5α-hydroxycholestane (XXX) as the product. While 3α-hydroxy-17β-acetoxy-5β-androstane (XXXI) gave 3α,9α-oxido-17β-acetoxy-5β-androstane (XXXII).

\[ \text{XXVI} \xrightarrow{\text{HOBr}} \text{XXVII} \xrightarrow{\text{Pb(OAc)}_4} \]

\[ \text{XXVIII} \]

\[ \text{XXIX} \xrightarrow{\text{Pb(OAc)}_4, \text{reflux}} \text{XXX} \]
Immer et al.\(^{24}\) showed the reaction of 3α-hydroxy-17β-acetoxy-Δ\(^{11}\)-5β-androstane (XXXIII) with lead (IV) acetate and they obtained 3α,9α-oxido-17β-acetoxy-Δ\(^{11}\)-5β-androstane (XXXIV).

Bowers and coworkers\(^{25}\) also studied the reaction of lead (IV) acetate with 3β-acetoxy-6β-hydroxytigogenin (XXXV) and reported the formation of 3β-acetoxy-6β,19-oxidotigogenin (XXXVI). 6β,19-Oxidoandrostane-3β,17β-diol diacetate (XXXVIII) was formed.
when androstane-3β,6β,17β-triol-3,17-diacetate (XXXVII) was treated with lead (IV) acetate\textsuperscript{26}.

\[
Pb(OAc)_{4} \xrightarrow{\phi H, \Delta} \text{(XXXVI)}
\]

\[
Pb(OAc)_{4} \xrightarrow{C_{6}H_{12}, CaCO_{3}, I_{2}, irrad^{-}} \text{(XXXVIII)}
\]

Bowers and Denot \textsuperscript{27} reported the reaction of 5β-pregn-3α,11β,20β-triol (XXXIX) with lead (IV) acetate and they obtained 5β-pregn-3α,20β-diol-11-one (XL), 5β-pregn-3α-acetoxy-20β-ol-11-one (XLI) and 3α,9α-oxido-5β-pregn-20β-ol-11-one (XLII) as the products.
Fieser and Stevenson\textsuperscript{28} carried out the reaction of lead (IV) acetate with 3-oxo cholest-5-ene (XLIII) for the formation of 3-oxo-4\alpha-acetoxysterol-5-ene (XLIV) and 3-oxo-6\alpha-acetoxysterol-5-ene (XLV) as the products.
Heusler et al.\textsuperscript{29} reported the reaction of (XLVI) with lead (IV) acetate to obtain (XLVII) and (XLVIII) as the products.

Reaction of 4\(\beta\)-hydroxy-17\(\beta\)-propionyloxy-5\(\alpha\)-androstan (XLIX), 4\(\beta\)-hydroxy-5-chloro-17\(\beta\)-propionyloxy-5\(\alpha\)-androstan (LI)\textsuperscript{29} and (XXVII)\textsuperscript{30} with lead (IV) acetate afforded 4\(\beta\),19-oxidolactone-17\(\beta\)-propionyloxy-5\(\alpha\)-androstan (L), 6\(\beta\),19-oxido-5-chloro-17\(\beta\)-propionyloxy-19-acetoxy-5\(\alpha\)-androstan (LII) and (LIII).
Meystre and coworkers reported the reaction of 5β-pregnan-3α-acetoxy-11β-hydroxy-20-one (LIV) with lead (IV) acetate in the presence of iodine and compounds (LV) and (LVI) as the
The reaction of lead (IV) acetate with cholest-5-ene (LVII), 3β-acetoxycholest-5-ene (LVIII), 3β-chlorocholest-5-ene (LIX) and 3β-hydroxycholest-5-ene (LX) in the presence of N-aminophthalimide gave 5α-cholestano[5,6-b]-N-phthalimidoaziridine (LXI), 3β-acetoxy-5α-cholestano[5,6-b]-N-phthalimidoaziridine (LXII), 3β-chloro-5α-cholestano[5,6-b]-N-phthalimidoaziridine (LXIII) and 3β-hydroxy-5α-cholestano[5,6-b]-N-phthalimidoaziridine (LXIV) as the products.32

products were obtained.
The reaction of 3,6-dinitrocholesta-3,5-diene (LXV) with lead (IV) acetate in presence of acetic acid afforded 3β-hydroxy-6-nitrocholesta-3,5-dien-4β-yl acetic acid lactone (LXVI), 3β-hydroxy-3,6-dinitrocholest-5-en-4β-yl acetic acid lactone (LXVII) and 3,6-dinitrocholesta-3,5-diene-7β-acetate (LXVIII) as the products.
The reaction of steroidal-6-oximes (LXIX - LXXI) with lead (IV) acetate gave nitrosoacetates (LXXII - LXXIV) and nitroacetates (LXXV - LXXVII)\textsuperscript{34,35} as the corresponding products.
REACTION OF STEROIDAL DIOLS WITH LEAD (IV) ACETATE:

A number of papers dealing with the syntheses of 6β, 19-oxidosteroids from steroidal bromohydrins, epoxides and hydroxy compounds have been cited in the literature. The synthesis of 3β-substituted 6β,19-oxido-5-hydroxy-5α-cholestane (LXXXI - LXXXIII) from their corresponding steroidal diols (LXXVIII - LXXX) with the reaction of lead (IV) acetate is reported here.
Reaction of 3β-chloro-5,6β-dihydroxy-5α-cholestan (LXXVIII) with Lead (IV) acetate: 3β-Chloro-6β,19-oxido-5-hydroxy-5α-cholestan (LXXXI)

3β-Chloro-5,6β-dihydroxy-5α-cholestan (LXXVIII) in dry benzene and a catalytic amount of iodine was heated with lead (IV) acetate under reflux for 10 hrs. The progress of the reaction was monitored by TLC. After the completion of the reaction the solvent was removed under reduced pressure and the residue thus obtained was taken in ether. The ethereal solution was washed with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave solid product which was recrystallized from methanol, m.p. 135°.

\[
\text{Pb(OAc)}_4, \text{C}_6\text{H}_6, \text{I}_2, \text{Reflux} \quad 80^\circ, \quad 10\text{hrs}
\]

Characterization of the compound, m.p. 135° as 3β-chloro-6β,19-oxido-5-hydroxy-5α-cholestan (LXXXI):

The elemental analysis of the compound, m.p. 135° corresponded to the molecular formula \( \text{C}_{27}\text{H}_{45}\text{O}_2\text{Cl} \). The IR spectrum
of the compound exhibited bands at 3430 (-OH), 2950 (C-H), 1240 (oxido linkage) and 730 cm⁻¹ (C-Cl). The ¹H-NMR spectrum of the compound exhibited broad signals centred at δ 5.3 and 2.1 integrating for one proton each and were assigned to C6α-H and C5α-OH respectively. A broad singlet centred at δ 4.1 integrating for two protons was also found in NMR spectrum and was assigned to C19-H₂. The multiplet centred at δ 3.5 integrating for one proton was exhibited for C3α-H (J = 16 Hz)³⁶. Angular and side chain methyl protons were observed at δ 0.73 (C13-CH₃), 0.95 and 0.85 (other methyl protons). These values suggested the compound to be 3β-chloro-6β,19-oxido-5-hydroxy-5α-cholestane (LXXXI). This structure was further supported by mass spectral studies. The mass spectrum of (LXXXI) gave the molecular ion peak at M⁺ 436/438 (C₂₇H₄₅O₂Cl) followed by other significant peaks at m/z 400, 385, 382, 367, 323/325, 272, 269, 121 and lower mass fragment ion peaks. Formation of some of the significant fragment ions has been rationalized in Scheme-1.

![Scheme-1](image-url)
Reaction of 3β-acetoxy-5,6β-dihydroxy-5α-cholestan (LXXIX) with lead (IV) acetate: 3β-Acetoxy-6β,19-oxido-5-hydroxy-5α-cholestan (LXXXII)

3β-Acetoxy-5,6β-dihydroxy-5α-cholestan (LXXIX) when dissolved in dry benzene was heated with lead (IV) acetate (catalytic amount of iodine) under reflux for 10 hrs. After the completion of the reaction, the solvent was removed under reduced pressure and residue was taken in ether and the ethereal layer was washed as described earlier. The removal of the solvent gave semi-solid which was crystallized from methanol to afford a compound, m.p. 101°.

Characterization of the compound, m.p. 101° as 3β-acetoxy-6β-19-oxido-5-hydroxy-5α-cholestan (LXXXII)

The compound, m.p. 101° was analyzed correctly for C_{29}H_{48}O_{4}. The IR spectrum of the compound exhibited bands at 3440 (-OH), 2940 (C-H), 1725, 1240 (CH_3COO) and 1225 cm^{-1}
(oxido linkage). The $^1$H-NMR spectrum of the compound displayed a broad signal at $\delta$ 5.2 integrating for one proton and was assigned to C6α-H. Another broad singlet was observed at $\delta$ 4.2 integrating for two protons which was assigned to C19-H$_2$ and a multiplet centred at $\delta$ 4.7 for C3α-H ($J = 18$ Hz)$^{37}$. The singlet at $\delta$ 2.2 was observed for one proton of C5α-CH and another singlet at $\delta$ 2.0 integrating for three protons was due to acetate methyl. Angular and side chain methyl protons were observed at $\delta$ 0.75 (C13-CH$_3$), 0.95 and 0.85. These values suggested the structure of the compound, m.p. 101° as 3β-acetoxy-6β,19-oxido-5-hydroxy-5α-cholestan-5a-ol (LXXXII). This structure was further supported by mass spectral data. The mass spectrum of the compound (LXXXII) gave an intense molecular ion peak at M$^+$ 460 ($C_{29}H_{48}O_4$). Other distinguishing fragment ion peaks were at m/z 400, 385, 382, 367, 347, 272, 269, 121 and lower mass fragment ion peaks. The formation pathways of some important fragment ions have been shown in Scheme-2.
Reaction of 3β-hydroxy-5,6β-dihydroxy-5α-cholestane (LXXX) with lead (IV) acetate: 3β-Hydroxy-6β,19-oxido-5-hydroxy-5α-cholestane (LXXXIII)

3β-Hydroxy-5,6β-dihydroxy-5α-cholestane (LXXX) in dry benzene and a catalytic amount of iodine was heated with lead (IV) acetate under reflux for 10 hrs. After the completion of the reaction, the solvent was removed under reduced pressure and the usual work up of the residue and purification by crystallization provided an oily compound.

Characterization of the compound, oil as 3β,5-dihydroxy-6β,19-oxido-5α-cholestane (LXXXIII)

Oily compound (LXXXIII) was analyzed correctly for C_{27}H_{46}O_{3}. The IR spectrum of the compound showed absorption bands at 3460-3400 (–OH), 2950 (C–H) and 1235 cm⁻¹ (oxido linkage). The $^1$H-NMR spectrum of the compound displayed a broad signal at δ 5.3 integrating for one proton which was assigned to C6α–H and other broad singlet at δ 4.2 for two protons of C19–H₂. A multiplet was observed at δ 3.4 for C3α–H.
A broad singlet was found between $\delta$ 2.3-2.1 for hydroxy protons at C3$\beta$-OH and C5$\alpha$-OH. Angular and side chain methyl protons were observed at $\delta$ 0.69 (C13-CH$_3$), 0.89 and 0.79. These values suggested the structure of the oily compound as 3$\beta$, 5-dihydroxy -6$\beta$,19-oxido-5$\alpha$-cholestan-1-one (LXXXIII). The compound (LXXXIII) on acetylation gave compound (LXXXII). The structure of compound (LXXXIII) was further supported by mass spectral data. The mass spectrum of the compound (LXXXIII) gave an intense molecular ion peak at $M^+$ 418 ($C_{27}H_{46}O_3$) followed by other significant peaks at m/z 400, 385, 382, 367, 305, 272, 269, 121 and lower mass fragment ion peaks. Genesis of some of the peaks has been given in Scheme-3.
REACTION OF STEROIDAL EPOXIDES WITH LEAD (IV) ACETATE

Reaction of lead (IV) acetate with steroidal epoxides and olefins are reported in literature. We have also selected few steroidal epoxides such as 5,6α-epoxy-5α-cholestane (LXXXIV) and its 3β-substituted analogues (LXXXV - LXXXVII) for the reaction with lead (IV) acetate to study the course of reaction which afforded hydroxyacetates (LXXXVIII, LXXXIX and XCII), and diacetates (XC and XCI). The structures of the compounds were established on the basis of spectral evidences and comparison with authentic samples in known cases.
Reaction of 5,6α-epoxy-5α-cholestan-3-one (LXXXIV) with lead (IV) acetate in acetic acid: 5-Hydroxy-6β-acetoxy-5α-cholestan-3-one (LXXXVIII) and 5,6β-diacetoxy-5α-cholestan-3-one (XC).

5,6α-Epoxy-5α-cholestan-3-one (LXXXIV) in glacial acetic acid was refluxed with lead (IV) acetate for 8 hrs. After completion of the reaction the solvent was removed under reduced pressure and the residue was extracted with ether. The ethereal layer was washed with water and dried. Evaporation of the solvent gave an oil which on column chromatography over silica gel provided a solid compound, m.p. 104° and an oily compound.
Characterization of the compound, m.p. 104° as 5-hydroxy-6β-acetoxy-5α-cholestane (LXXXVIII)

The compound (LXXXVIII) m.p. 104° was correctly analyzed for C_{29}H_{49}O_3. The presence of hydroxy group was revealed by the strong band at 3450 cm\(^{-1}\) in its IR spectrum, the other characteristic bands were at 1735 (acetate) and 1240 and 1060 cm\(^{-1}\) (C-O). Its \(^1\)H-NMR spectrum exhibited a multiplet at \(\delta\) 4.6 for C\(6\alpha\)-H (\(W^1/2 = 7\) Hz) and a singlet was observed at \(\delta\) 2.0 for the three protons of acetoxy group. The angular and side chain methyl protons appeared at \(\delta\) 1.1 (\(\text{Cl}0\)-CH\(_3\)), 0.68 (\(\text{Cl}3\)-CH\(_3\)), 0.90 and 0.85 (other methyl protons). In the light of above discussion the compound, m.p. 104° may therefore be regarded as 5-hydroxy-6β-acetoxy-5α-cholestane (LXXXVIII).

Characterization of the oily compound as 5,6β-diacetoxy-5α-cholestane (XC)

The oily compound (XC) was correctly analyzed for C\(_{31}\)H\(_{52}\)O\(_4\). Its IR spectrum exhibited the bands at 1735, 1730 (two acetate >C=O) and 1240, 1200, 1040 and 1035 cm\(^{-1}\) (C-O). Its \(^1\)H-NMR spectrum exhibited a multiplet centred at \(\delta\) 4.6 for C\(6\alpha\)-H (\(W^1/2 = 8\) Hz). The signals for acetoxy methyl protons were observed at \(\delta\) 2.05 and 1.95. The methyl signals were appeared at \(\delta\) 1.1 (\(\text{Cl}0\)-CH\(_3\)), 0.68 (\(\text{Cl}3\)-CH\(_3\)), 0.92 and 0.80. In the light of above discussion the oily compound was characterized as 5,6β-diacetoxy-5α-cholestane (XC).
Reaction of $3\beta$-chloro-5,6α-epoxy-5α-cholestane (LXXXV) with lead (IV) acetate in acetic acid: $3\beta$-Chloro-5-hydroxy-6β-acetoxy-5α-cholestane (LXXXIX) and $3\beta$-chloro-5,6β-diacetoxy-5α-cholestane (XCI)

$3\beta$-Chloro-5,6α-epoxy-5α-cholestane (LXXXV) in glacial acetic acid was refluxed with lead (IV) acetate for 8 hrs. After the completion of the reaction, the reaction mixture after usual work up and chromatography over silica gel provided two compounds, m.ps. 137° and 112°.

The compound (LXXXIX) m.p. 137° was correctly analyzed for $C_{29}H_{49}O_3\text{Cl}$ (positive Beilstein test). Its IR spectrum exhibited a strong broad band at 3410 cm$^{-1}$. The other characteristic bands were at 1730, (acetate >C=O) and 1260,
1030 cm$^{-1}$ (C-O). Its $^1$H-NMR spectrum exhibited a multiplet at $\delta$ 5.4 for C6α-H ($W_\frac{1}{2} = 7$ Hz) and multiplet centred at $\delta$ 4.02 integrating for one proton to C3α-H ($W_\frac{1}{2} = 18$ Hz)\textsuperscript{36}. The signal at $\delta$ 2.05 integrating for three protons was due to acetate methyl. Angular and side chain methyl protons were observed at 1.28 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.92 and 0.80. In the light of above discussion the compound m.p. 137$^\circ$ may therefore, be characterized as 3β-chloro-5-hydroxy-6β-acetoxy-5α-cholestane (LXXXIX).

Characterization of the compound, m.p. 112$^\circ$ as 3β-chloro-5, 6β-diaceotoxy-5α-cholestane (XCl)

The compound (XCl) m.p. 112$^\circ$ was correctly analyzed for C$_{31}$H$_{51}$O$_4$Cl (positive Beilstein test). The IR spectrum of the compound exhibited bands at 1740, 1735 (two acetate $\geq$C=O), 1240, 1050 (C-O) and 760 cm$^{-1}$ (C-Cl). The $^1$H-NMR spectrum of the compound displayed multiplet at $\delta$ 4.75 for C6α-H ($W_\frac{1}{2} = 8$ Hz) and a multiplet centred at $\delta$ 4.02 integrating for one proton to C3α-H ($W_\frac{1}{2} = 16$ Hz)\textsuperscript{36}. The two singlets at $\delta$ 2.0 and 1.9 were for two acetate methyl protons. Angular and side chain methyl protons were observed at $\delta$ 1.28 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.90 and 0.80. In the light of above discussion the compound m.p. 112$^\circ$ may be characterized as 3β-chloro-5,6β-diaceotoxy-5α-cholestane (XCl).
Reaction of 3β-hydroxy-5,6α-epoxy-5α-cholestane (LXXXVI) with lead (IV) acetate in acetic acid: 3β-Acetoxycholest-5-ene (LVIII) and 3β,5-diacetoxy-6β-hydroxy-5α-cholestane (XCII)

3β-Hydroxy-5,6α-epoxy-5α-cholestane (LXXXVI) in glacial acetic acid was refluxed with lead (IV) acetate for 8 hrs. After completion of the reaction the reaction mixture was worked up in ether and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which on column chromatography over silica gel provided two compounds of m.ps. 96° and 116°.

\[
\text{HO} \quad \text{Pb(OAc)}_4 \quad \text{LCOH,ACOK} \quad \text{Reflux,8hrs}
\]

Characterization of the compound m.p. 116° as 3β-acetoxycholest-5-ene (LVIII)

The compound m.p. 116° (LVIII) was correctly analyzed for \( C_{29}H_{48}O_2 \). The IR spectrum of the compound showed bands at 1735 (CH\(_3\)COO), 1625 (C=C) and 1235 and 1050 cm\(^{-1}\) (C-O). The \(^1\)H-NMR
The acetate methyl protons appeared at δ 2.0. Angular and side chain methyl protons were observed at δ 1.1 (Cl0-CH₃), 0.70 (Cl3-CH₃), 0.90 and 0.80. In the light of above discussion the compound, m.p. 116° was identified as 3β-acetoxycholest-5-ene (LVIII). This compound (LVIII) was found identical with the authentic sample of 3β-acetoxycholest-5-ene.

**Characterization of the compound, m.p. 96° as 3β,5-diacetoxy-6β-hydroxy-5α-cholestan (XCII)**

The compound m.p. 96° (XCII) was correctly analyzed for C₃₁H₅₂O₅. The presence of hydroxy group is revealed by the strong absorption band at 3410 cm⁻¹. In the IR spectrum the other characteristic bands were at 1740, 1735 (acetate >C=O) 1235 and 1060 cm⁻¹. The ¹H-NMR spectrum of the compound displayed a broad signal at δ 5.4 for one proton which was assigned to C6α-H (W₁/₂ = 8 Hz) and other broad multiplet centered at δ 3.94 for C3α-H (W₁/₂ = 16 Hz)³⁶. The acetate methyl protons were observed at 2.0 and 1.9. Angular and side chain methyl protons were observed at δ 1.1 (Cl0-CH₃), 0.70 (Cl3-CH₃), 0.90 and 0.80. In the light of above discussion the compound, m.p. 96° may therefore, be characterized as 3β,5-diacetoxy-6β-hydroxy-5α-cholestan (XCII).
Reaction of 3β-acetoxy-5,6α-epoxy-5α-cholestan (LXXXVII) with lead (IV) acetate in acetic acid: 3β-Acetoxycholest-5-ene (LVIII) and 3β,5-diacetoxy-6β-hydroxy-5α-cholestan (XCII)

3β-Acetoxy-5,6α-epoxy-5α-cholestan (LXXXVII) in glacial acetic acid when treated under reflux with lead (IV) acetate provided two compounds, m.p. 96° and 116°.

The compound, m.p. 116° was found similar to 3β-acetoxycholest-5-ene (LVIII) and compound m.p. 96° was found identical in all respects (m.p., m.m.p., IR and $^1$H-NMR) with 3β,5-diacetoxy-6β-hydroxy-5α-cholestan (XCII). The compounds (LVIII) and (XCII) were obtained earlier when 3β-hydroxy-5,6α-epoxy-5α-cholestan (LXXXVI) was treated with lead (IV) acetate.
In continuation to our previous studies\textsuperscript{34,35} and related work elsewhere on the reactions of lead (IV) acetate with steroidal ketoximes, we carried out the reaction of lead (IV) acetate with $3\beta,5$-dihydroxy-$5\alpha$-cholestan-6-one oxime (XCIII) and its $3\beta$-chloro (XCIV) and acetoxy (XCV) analogues which provided steroidal ketones (XCVI and XCVII), hydroxyketone (XCVIII), N-acetyl derivatives (C-CII) and $\alpha$-acetylated hydroxyketone (XCIX). The structures of these compounds were established on the basis of spectral evidences and comparison with authentic samples in known cases.

\[ \text{Pb(OAc)}_4 \xrightarrow{\text{Dry } C_6H_6, \text{AcOH}} \]

\[ (\text{XCIII}) \quad R \quad (\text{XCIV}) \quad \text{Cl} \\
(\text{XCV}) \quad OAc \]

\[ (\text{XCVI}) \quad R \quad (\text{XCVII}) \quad \text{Cl} \]

\[ (\text{XCVIII}) \quad \text{OAc} \]

\[ (\text{XCIX}) \quad R \]

\[ (\text{C}) \quad \text{OH} \\
(\text{CI}) \quad \text{Cl} \\
(\text{CII}) \quad \text{OAc} \]
Reaction of 3β,5-dihydroxy-5α-cholestan-6-one oxime (XCIII) with lead (IV) acetate in benzene and acetic acid: 3β-Acetoxycholesten-4-en-6-one (XCVI), 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (XCVIII) and 3β,5-dihydroxy-5α-cholestan-6-N-acyloxime (C)

Lead (IV) acetate was added portion wise to a stirred solution of oxime (XCIII) in dry benzene and acetic acid. The mixture was stirred at room temperature for 2 hrs. The progress of the reaction was monitored by TLC and the solvent was removed under reduced pressure. The residue was taken up in ether and the solution was washed successively with water, sodium bicarbonate solution (5%) and again with water. The ethereal layer was dried over anhydrous sodium sulphate. The removal of the solvent provided an oil which on column chromatography over silica gel afforded three compounds m.ps, 107°, 238° and 176°.
Identification of the compound, m.p. 107° as 3β-acetoxycholest-4-en-6-one (XCVI)

The compound (XCVI) m.p. 107° was correctly analysed for C₂₉H₄₆O₃. The presence of acetate group is revealed by the strong band at 1740 cm⁻¹ in its IR spectrum which also exhibited other characteristic bands at 1680 (C=O), 1625 (C=C), 1240 and 1040 cm⁻¹ (C-O). Its ¹H-NMR spectrum exhibited a broad singlet at δ 5.4 for (C₄-H) and a multiplet centered at δ 4.5 for C₃α-H (W½ = 18 Hz). A singlet was also observed at δ 2.0 for three protons of acetoxy group. The angular and side chain methyl protons appeared at δ 1.1 (C₁₀-CH₃), 0.75 (C₁₃-CH₃), 0.90 and 0.80 (other methyl protons). In the light of above discussion the compound, m.p. 107° may therefore be regarded as 3β-acetoxycholest-4-en-6-one (XCVI) which was found identical with authentic sample of 3β-acetoxycholest-4-en-6-one (m.p., m.m.p., IR and NMR).

Identification of the compound, m.p. 238° as 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (XCVIII)

The compound, m.p. 238° was correctly analyzed for C₂₉H₄₈O₄. Its IR spectrum gave bands at 3400 (O-H), 1735 (CH₃COO), 1680 (C=O), 1150 and 1020 cm⁻¹ (C-O). The ¹H-NMR spectrum of the compound exhibited a multiplet centered at δ 4.02 (C₃α-H; W½ = 16 Hz), and a singlet at δ 2.15 for (C₅α-OH). Another singlet for acetate methyl was observed at δ 2.1. The angular and side chain methyl protons appeared at δ 1.20 (C₁₀-CH₃)
0.75 (Cl3-CH3), 0.95 and 0.85. In the light of above discussion and comparison with the authentic sample the compound, m.p. 238° in the light of above discussion and comparison with the authentic sample may therefore be regarded as 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (XCVIII).

Characterization of the compound, m.p. 176° as 3β,5-hydroxy-5α-cholestan-6-N-acyloxime (C)

The compound, m.p 176° was correctly analyzed for C_{29}H_{49}O_{4}N. Its IR spectrum gave bands at 3350 (2X-OH), 1725 (CH₃COO-), 1680 (C=N), 1210 and 1050 cm⁻¹ (C-O). The ¹H-NMR spectrum of the compound exhibited a multiplet centered at δ 3.8 for C3α-H (W_{2} = 16 Hz) and a singlet at δ 2.15 for(C5α-OH). The acetate methyl protons were observed at δ 1.9 as a singlet. Angular and side chain methyl protons appeared at δ 1.20 (Cl0-CH₃), 0.75 (Cl3-CH₃), 0.95 and 0.85. In the light of above discussion the compound, m.p. 176° may therefore be formulated as 3β,5-hydroxy-5α-cholestan-6-N-acyloxime (C).

Reaction of 3β-chloro-5-hydroxy-5α-cholestan-6-one oxime (XCIV) with lead (IV) acetate in benzene and acetic acid : 3β-Chlorocholest-4-en-6-one (XCVII), 3β-chloro-7α-acetoxy-5-hydroxy-5α-cholestan-6-one (XCIX) and 3β-chloro-5-hydroxy-5α-cholestan-6-N-acyloxime (CI)

Lead (IV) acetate was added in portions to a stirred solution of oxime (XCIV) in dry benzene and acetic acid. The mixture was
stirred at room temperature for 2 hrs. and after completion of the reaction, the reaction mixture was worked up as described earlier. The oil obtained was chromatographed over silica gel to afford two solids, m.ps. $163^\circ$, $87^\circ$ and an oily product.
Identification of the compound, m.p. 163° as 3β-chlorocholest-4-en-6-one (XCVII)

The compound, m.p. 163° (positive Beilstein test) was correctly analyzed for C_{27}H_{44}OCl. The IR spectrum of the compound exhibited bands at 1680 (C=O) and 1625 (C=C) and 760 cm^{-1} (C-Cl). The $^1$H-NMR spectrum of the compound gave broad singlet at $\delta$ 5.4 (C4-H) and a multiplet centred at $\delta$ 3.8 for C3α-H ($W_2^1 = 16$ Hz). The angular and side chain methyl protons were observed at $\delta$ 1.20 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.95 and 0.85.

In the light of above discussion the compound, m.p. 163° may therefore be identified as 3β-chlorocholest-4-en-6-one (XCVII), which was found identical with authentic sample of 3β-chlorocholest-4-en-6-one (m.p., m.m.p., IR and NMR).

Identification of the compound, m.p. 87° as 3β-chloro-7α-acetoxv-5-hydroxy-5α-cholestan-6-one (XCIX)

The compound, m.p. 87° (positive Beilstein test) was correctly analyzed for C_{29}H_{47}O$_4$Cl. The IR spectrum of the compound gave bands at 3500 (-OH) and at 1735 cm^{-1} for (CH$_3$COO-) groups. The ketonic function at C6-position was appeared at 1690 cm^{-1} (C=O) and bands at 1240 and 1040 cm^{-1} for (C-O). The C-Cl band appeared at 750 cm^{-1}. The $^1$H-NMR spectrum of the compound exhibited broad singlets at $\delta$ 4.7 ($W_2^1 = 5$ Hz) and 2.3 for (C7β-H) and C5α-OH, respectively and a multiplet centred at $\delta$ 3.4 for C3α-H ($W_2^1 = 16$ Hz). The acetate methyl protons were observed at $\delta$ 2.05. Angular and side chain methyl protons were
appeared at $\delta$ 1.20 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.95 and 0.85. The above discussion confirmed the compound, m.p. 87° as 3β-chloro-7α-acetoxy-5-hydroxy-5α-cholestan-6-one (XCIX).  

Characterization of the compound (oil) as 3β-chloro-5-hydroxy-5α-cholestan-6-N-acyloxime (CI)  

The oily compound (CI) (positive Beilstein test) was correctly analyzed for C$_{29}$H$_{48}$O$_3$NCl. IR spectrum of the compound gave bands at 3450 cm$^{-1}$ (-OH), 1745 (CH$_3$COO-), 1560 (C=N), 1240, 1020 (C=O) and 760 cm$^{-1}$ (C-Cl). The $^1$H-NMR spectrum of the compound exhibited a multiplet centered at $\delta$ 3.4 for C3α-H ($J/2 = 18$ Hz) and a singlet at $\delta$ 2.4 due to (C5α-OH). The acetate methyl protons were observed as singlet at $\delta$ 2.0. Angular and side chain methyl protons appeared at $\delta$ 1.20 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.95 and 0.85. On the basis of above facts the oily compound was characterized as 3β-chloro-5-hydroxy-5α-cholestan-6-N-acyloxime (CI).  

Reaction of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one oxime (XCV) with lead (IV) acetate in benzene and acetic acid: 3β-Acetoxycholest-4-en-6-one (XCVI), 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (XCVIII) and 3β-acetoxy-5-hydroxy-5α-cholestan-6-N-acyloxime (CII)  

Lead (IV) acetate was added in portions to a stirred solution of oxime (XCV) in dry benzene and acetic acid. The
mixture was stirred at room temperature for 2 hrs. and after completion of the reaction the reaction mixture was worked up as described in previous experiments. The oil obtained was chromatographed over silica gel to furnish three compounds, m.ps. $106^\circ$, $238^\circ$ and an oil.

The compounds m.p. $106^\circ$ and $238^\circ$ were identified as (XCVI) and (XCVIII), respectively on the basis of comparison with the samples obtained earlier and the authentic samples.
Characterization of oily compound as 3β-acetoxy-5-hydroxy-5α-cholestan-6-N-acyloxime (CII)

The oily compound was correctly analyzed for $C_{31}H_{51}O_5N$. IR spectrum of the compound gave bands at 3400 (−OH), 1735, 1715 (2XCH$_3$COO−), 1660 (C=N), 1240 and 1060 cm$^{-1}$ (C−O). The $^1$H-NMR spectrum of the compound exhibited a multiplet centred at $\delta$ 4.45 for C3α−H ($\Delta\nu_2 = 16$ Hz). The C5α-hydroxy proton singlet was observed at $\delta$ 2.2. The two acetate methyl protons were observed at $\delta$ 2.1 and 2.0 (2 x CH$_3$COO−). Angular and side chain methyl appeared at 1.20 (Cl0−CH$_3$), 0.75 (Cl3−CH$_3$), 0.95 and 0.85. On the basis of above evidences the oily compound was characterized as 3β-acetoxy-5-hydroxy-5α-cholestan-6-N-acyloxime (CII).
Experimental

Reaction of 3β-chloro-5,6β-dihydroxy-5α-cholestan-5α-cholestane (LXXVIII) with lead (IV) acetate: 3β-Chloro-6β,19-oxido-5-hydroxy-5α-cholestan-5α-cholestane (LXXXI)

Lead (IV) acetate (5.6 g; 11.3 m mol) was added in portions in the presence of iodine (1 g) to the solution of the diol (LXXVIII) (2.0 g; 4.54 m mol) in dry benzene (90 ml). The reaction mixture was refluxed for 10 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction the solvent was removed under reduced pressure and the residue, thus obtained, was taken in ether. The ethereal solution was washed with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave a solid which was recrystallized from methanol to provide 3β-chloro-6β,19-oxido-5-hydroxy-5α-cholestan-5α-cholestane (LXXXI) (1.0 g; 2.10 m mol), m.p. 135°.

Analysis Found : C, 74.10; H, 10.40
C₂₇H₄₅O₂Cl requires : C, 74.1; H, 10.5%.
IR : $\nu_{\text{max}}$. 3430 (OH), 2950 (C-H), 1240 (oxido linkage) and 730 cm$^{-1}$ (C-Cl).

$^1$H-NMR : $\delta$ 5.3 (br, 1H, C6α-H), 4.1 (brs, 2H, C19-H$_2$), 3.5 (mc, 1H, $W^2_2 = 16$ Hz; C3α-H), 2.1 (brs, 1H, C5α-OH), 0.73 (C13-CH$_3$), 0.95 and 0.85 (other methyl protons).

MS : 436/438 (13/3.99; C$_{27}$H$_{45}$O$_2$Cl), 400 (86.45; C$_{27}$H$_{44}$O$_2$), 393 (1.33), 392 (4.66), 391 (5.32), 390 (9.31), 388 (11.97), 386 (26.60), 385 (53.20), 382 (13.30), 377 (1.33), 376 (2.66), 375 (3.99), 374 (2.66), 373 (2.66), 372 (5.32), 370 (9.31), 367 (6.99), 366 (0.68), 365 (3.99), 364 (2.66), 363 (6.65), 362 (3.99), 361 (7.98), 360 (2.66), 352 (0.68), 351 (2.66), 350 (3.99), 349 (5.32), 348 (5.32), 347 (6.65), 346 (2.66), 345 (3.99), 340 (0.68), 337 (1.33), 336 (2.66), 335 (20.10), 334 (70.49), 332 (5.32), 331 (2.66), 330 (1.33), 323/325 (12.33/3.99), 322 (1.33), 321 (1.33), 320 (13.30), 319 (6.65), 318 (5.32), 316 (2.66), 311 (3.99), 310 (19.95), 309 (85.12), 308 (26.60), 307 (5.32), 306 (2.66), 305 (1.33), 304 (1.22), 298 (3.99), 297 (13.30), 296 (6.56), 295 (2.66), 294 (1.33), 293 (3.99), 292 (1.33), 291 (1.33), 290 (5.32), 289 (1.33), 282 (5.32), 281 (19.95), 280 (15.96), 279 (13.30), 278 (51.87), 276 (6.65), 275 (6.65), 274 (3.99), 272 (2.66), 271 (1.33), 270 (1.33), 269 (2.66), 268 (3.99),
Reaction of 3\(\beta\)-acetoxv-5,6\(\beta\)-dihydroxv-5\(\alpha\)-cholestane (LXXXIX) with lead (IV) acetate : 3\(\beta\)-Acetoxv-6\(\beta\),19-oxido-5-hydroxy-5\(\alpha\)-cholestan (LXXXII)

Lead (IV) acetate (5.6 g, 11.3 m mol) was added in portions in the presence of catalytic amount of iodine to 3\(\beta\)-acetoxv-5,6\(\beta\)-dihydroxv-5\(\alpha\)-cholestane (LXXXIX) (2.0 g, 4.33 m mol) dissolved in dry benzene (90 ml) and the reaction mixture was refluxed under similar reaction conditions as described in the previous reaction. The reaction mixture after usual work up and crystallization from methanol afforded 3\(\beta\)-acetoxv-6\(\beta\),19-oxido-5-hydroxy-5\(\alpha\)-cholestan (LXXXII) (1.05 g, 1.90 m mol), m.p. 101°.

Analysis Found : C, 75.60; H, 10.50

\(\text{C}_{29}\text{H}_{48}\text{O}_{4}\) requires : C, 75.6; H, 10.5%.
IR : $\nu_{\text{max}}$ 3440 ($\text{OH}$), 2940 ($\text{C-H}$), 1725, 1240 ($\text{CH}_3\text{COO}^-$) and 1225 cm$^{-1}$ (oxido linkage).

$^1$H-NMR : $\delta$ 5.2 (br, 1H, C6a-H), 4.7 (mc, 1H, $\nu = 18$ Hz; C3a-H), 4.2 (brs, 2H, C19-H$_2$), 2.2 (s, 1H, C5a-OH), 2.0 (s, CH$_3$COO$^-$), 0.75 (C13-CH$_3$), 0.95 and 0.85 (other methyl protons).

MS : 460(13.30; C$_{29}$H$_{48}$O$_4$), 400(5.32; C$_{27}$H$_{44}$O$_2$), 399(6.65), 398 (2.66), 397(5.32), 387(2.66), 386(66.50), 385(94.43), 384 (95.76), 382(29.26), 381(6.55), 380(2.66), 371(1.33), 370 (0.68), 368(3.99), 367(33.25), 366(100.00), 355(2.66), 354 (3.99), 353(2.66), 352(2.01), 350(2.66), 347(29.26), 339(3.99),
338(9.31), 336(9.31), 335(15.96), 334(2.66), 329(1.33), 328 (1.33), 325 (3.99), 324(5.32), 323 (1.33), 311 (2.66), 310 (26.60), 309 (75.81), 308(4.32), 307 (1.33), 306 (2.01), 305 (1.33), 285 (29.26), 284 (93.10), 283 (29.26), 282 (44.25),
281 (2.66), 280 (2.66), 272 (19.95), 271 (39.90), 270 (10.64),
269 (15.96), 268 (19.95), 267 (75.81), 266 (2.66), 265 (2.66), 261 (1.33), 260 (19.95), 259 (19.95), 258 (57.19),
257 (19.95), 256 (15.96), 249 (13.30), 248 (1.33), 247 (3.99),
240 (2.66), 239 (9.31), 238 (15.96), 237 (42.56), 236 (6.65),
235 (15.96), 234 (15.96), 233 (13.30), 232 (13.30), 230 (1.33), 229 (1.33), 226 (9.31), 224 (6.65), 223 (4.32), 221
Reaction of 3β-hydroxy-5,6β-dihydroxy-5α-cholestane (LXXX) with lead (IV) acetate: 3β,5-Dihydroxy-6β,19-oxido-5α-cholestane (LXXXIII)

Lead (IV) acetate (5.6 g, 11.3 m mol) was added in portions
in the presence of catalytic amount of iodine to 3β,5-dihydroxy-
5α-cholestane (LXXX) (2.0 g, 4.78 m mol) dissolved in dry benzene
(90 ml) and the reaction mixture was refluxed under the similar
reaction conditions, described in the previous reactions. After
usual workup and crystallization from methanol 3β,5-dihydroxy-
6β,19-oxido-5α-cholestane (LXXXIII) was obtained as an oil
(0.90 g, 1.90 m mol).

Analysis Found
C27H46O3 requires

IR

1H-NMR

MS : 418 (1.29; C27H46O3), 400 (6.45), 399 (19.35), 398 (51.60),
397 (7.74), 396 (9.03), 394 (3.87), 385 (1.29), 384
(2.58), 383 (7.74), 382 (10.32), 381 (3.87), 380 (6.45),
379 (9.03), 378 (2.58), 376 (2.58), 373 (2.58), 371 (2.58),
368 (2.58), 367 (15.48), 364 (1.29), 359 (3.87), 337 (5.16),
326 (2.58), 325 (6.45), 324 (1.29), 322 (1.29), 320 (1.29),
316 (3.87), 314 (6.45), 312 (2.58), 310 (2.58), 308 (3.87),
306 (3.87), 305 (12.90), 302 (1.29), 298 (2.58), 297 (5.16),
296 (6.45), 295 (2.58), 294 (3.87), 293 (1.29), 292 (2.58),
223:

290 (3.87), 289 (3.87), 288 (3.87), 287 (3.87), 286 (7.74), 285 (1.29), 284 (2.58), 282 (2.58), 280 (7.74), 279 (1.29), 278 (3.87), 277 (2.58), 276 (7.74), 275 (6.45), 274 (6.45), 273 (15.48), 272 (9.03), 271 (5.16), 270 (5.16), 269 (7.74), 268 (5.16), 267 (2.58), 266 (1.29), 265 (2.58), 264 (1.29), 263 (1.29), 262 (1.29), 261 (5.16), 260 (1.29), 259 (3.87), 258 (1.29), 257 (3.87), 256 (1.29), 255 (6.45), 254 (5.16), 253 (12.90), 252 (5.16), 251 (9.03), 250 (6.45), 249 (5.16), 248 (2.58), 247 (3.87), 246 (2.58), 245 (3.87), 244 (2.58), 243 (3.87), 242 (1.29), 241 (2.58), 240 (1.29), 239 (3.87), 238 (3.87), 237 (6.45), 236 (6.45), 235 (16.77), 234 (3.87), 233 (6.45), 232 (5.16), 231 (5.16), 230 (6.45), 229 (5.16), 228 (5.16), 227 (2.58), 226 (3.87), 225 (2.58), 224 (5.16), 223 (2.58), 222 (5.16), 221 (3.87), 220 (5.16), 219 (3.87), 218 (6.45), 217 (3.87), 216 (7.74), 215 (6.45), 214 (14.19), 213 (7.74), 212 (6.45), 211 (5.16), 210 (5.16), 209 (6.45), 208 (5.16), 207 (2.58), 206 (5.16), 205 (3.87), 204 (6.45), 203 (3.87), 202 (6.45), 201 (6.45), 200 (9.03), 199 (6.45), 198 (7.74), 197 (6.45), 196 (10.32), 195 (5.16), 194 (7.74), 193 (3.87), 192 (9.03), 191 (9.03), 190 (7.74), 189 (5.16), 188 (9.03), 187 (6.45), 186 (10.32), 185 (5.16), 184 (9.03), 183 (5.16), 182 (5.16), 181 (7.74), 180 (6.45), 179 (12.90), 178 (7.74), 177 (9.03), 176 (3.87), 175 (9.03), 174 (6.45), 173 (11.61), 172 (5.16), 171 (14.19), 170 (5.16), 169 (10.32), 168 (5.16), 167 (11.61), 166 (6.45), 165 (15.48), 164 (7.74), 163 (14.19), 162 (7.74), 161 (14.19), 160 (6.45), 159 (12.90), 158 (5.16), 157 (9.03), 156 (11.61), 155 (16.77), 154 (10.32), 153
Reaction of 5,6α-epoxy-5α-cholestanate (LXXXIV) with lead (IV) acetate: 5-Hydroxy-6β-acetoxy-5α-cholestanate (LXXXVIII) and 5,6β-diacetoxy-5α-cholestanate (XC)

5,6α-Epoxy-5α-cholestanate (LXXXIV) (2 g, 5.18 m mol), lead (IV) acetate (1.1 g, 2.24 m mol) and anhydrous potassium acetate (1 g) were refluxed in glacial acetic acid (150 ml) for 8 hrs. The reaction mixture was cooled to room temperature, diluted with ice-cold water and extracted with ether. The ethereal solution was washed with sodium bicarbonate solution (5%) and
water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Elution with light petroleum ether : ether (1:3) yielded (LXXXVIII) as solid compound which was crystallized from methanol (600 mg, 1.21 m mol) (m.p. 104°).

Analysis Found : C, 81.88; H, 11.01

C_{29}H_{49}O_3 requires : C, 81.9; H, 11.0%. 

IR : $\nu_{\text{max}}$ 3450 (br, $\text{O}-\text{H}$), 1735 (CH$_3$COO), 1240 and 1060 cm$^{-1}$ (C=O).

$^1$H-NMR : $\delta$ 4.6 (mc, C6α-H), 2.0 (s, CH$_3$COO-), 1.1 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.90 and 0.85 (other methyl protons).

Further elution with ether furnished the compound (XC) (400 gm, 0.820 m mol) as non-crystallizable oil.

Analysis Found : C, 76.25; H, 10.65

C$_{31}$H$_{52}$O$_4$ requires : C, 76.3; H, 11.0%

IR : $\nu_{\text{max}}$. 1735, 1730 (2 x CH$_3$COO-), 1240 and 1035 cm$^{-1}$ (C=O),

$^1$H-NMR : $\delta$ 4.6 (mc, C6α-H, $\nu_{\frac{1}{2}} = 8$ Hz), 2.05 and 1.95 (s, acetate protons), 1.1 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.92 and 0.80 (other methyl protons).

Reaction of 3β-chloro-5,6α-epoxy-5α-cholestanate (LXXXV) with lead (IV) acetate : 3β-Chloro-5-hydroxy-6β-acetoxy-5α-cholestanate (LXXXIX) and 3β-chloro-5,6β-diacetoxy-5α-cholestanate (XCI)

A mixture of 3β-chloro-5,6α-epoxy-5α-cholestanate (LXXXV)
(2.0 g, 4.96 m mol), lead (IV) acetate (1.1 g, 2.24 m mol) and anhydrous potassium acetate (1.0 g) was refluxed in glacial acetic acid (150 ml) for 8 hrs. The reaction mixture was cooled to room temperature, diluted with ice-cold water and extracted with ether. The ethereal solution was washed with sodium bicarbonate solution (5%) and water and dried over anhydrous sodium sulphate. Evaporation of the solvent left a residue which was chromatographed over silica gel (40 gm). Elution with light petroleum ether : ether (1:3) furnished the compound (LXXXIX) recrystallized from methanol (450 mg, 0.93 m mol), m.p. 137°.

Analysis Found : C, 72.42; H, 10.19
C_{29}H_{49}O_{3}Cl requires : C, 72.4; H, 10.2%.

IR : \( \nu_{\text{max}} = 3410 \text{ (br, 3°-OH)}, 1730 \text{ (CH}_3\text{COO-)}, 1260 \text{ and 1030 cm}^{-1} \text{ (C-O) and 760 cm}^{-1} \text{ (C-Cl)}. \)

\(^1\text{H-NMR} : \delta 5.4 \text{ (mc, C6}\alpha-H, W_2/2 = 7\text{Hz}), 4.02 \text{ (mc, C3}\alpha-H, W_2/2 = 18\text{Hz}), 2.05 \text{ (s, CH}_3\text{COO-)}, 1.28 \text{ (C10-CH}_3\text{)}, 0.68 \text{ (C13-CH}_3\text{), 0.90 and 0.80 (other methyl protons).} \)

Further elution with ether yielded (XCI) as a semi-solid which was crystallized from methanol (400 mg, 0.820 m mol), m.p. 112°.

Analysis Found : C, 71.49; H, 9.92
C_{31}H_{51}O_{4}Cl requires : C, 71.4; H, 9.9%.
IR : $\nu_{\text{max.}}$ 1740, 1735 (2 x CH$_3$COO$^-$), 1240, 1050 (C=O) and 760 cm$^{-1}$ (C-C1).

$^1$H-NMR : $\delta$ 4.75 (mc, C6a-H, $J_{1/2} = 8$ Hz), 4.02 (mc, C3a-H, $J_{1/2} = 16$ Hz), 2.0, 1.9 (s, acetate protons), 1.28 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.90 and 0.80 (other methyl protons).

**Reaction of 3$\beta$-hydroxy-5,6$\alpha$-epoxy-5$\alpha$-cholestan-6-one (LXXXVI) with lead (IV) acetate : 3$\beta$-Acetoxycholest-5-ene (LVIII) and 3$\beta$,5-diacycloxy-6$\beta$-hydroxy-5$\alpha$-cholestan-6-one (XCII)**

3$\beta$-Hydroxy-5,6$\alpha$-epoxy-5$\alpha$-cholestan-6-one (LXXXVI) (2.0 g, 5.00 m mol), lead (IV) acetate (1.1 g, 2.24 m mol) and anhydrous potassium acetate (1 g) were refluxed in glacial acetic acid (150 ml) for 8 hrs. The reaction mixture was cooled to room temperature, diluted with ice-cold water and extracted with ether. The ethereal solution was then washed with sodium bicarbonate solution (5%), water and dried over anhydrous sodium sulphate. Evaporation of the solvent left a residue which was chromatographed over silica gel (40 g). Elution with light petroleum ether : ether (1:3) furnished (LVIII) as a solid which was recrystallized from methanol (500 mg, 1.15 m mol) m.p. and m.m.p. 37 116$^\circ$.

Analysis Found : C, 81.31; H, 11.21

C$_{29}$H$_{48}$O$_2$ requires : C, 81.3; H, 11.2%.

IR : $\nu_{\text{max.}}$ 1735 (CH$_3$COO$^-$), 1625 (C=C), 1235 and 1050 cm$^{-1}$ (C-O).
Further elution with ether furnished the compound (XClII) which was recrystallized from methanol (600 mg, 1.20 m mol) m.p. 96°.

Analysis Found : C, 73.80; H, 10.32

\[ C_{31}H_{52}O_5 \] requires : C, 73.8; H, 10.3%.

IR : \( \nu_{max} \) 3410 (br, 3°-OH), 1740, 1735 (2 x CH\textsubscript{3}COO\textsuperscript{-}), 1225, and 1060 cm\textsuperscript{-1} (C-O).

\[ ^1H-NMR : \delta \ 5.45 \ (br, \ C6\alpha-H), \ 4.71 \ (mc, \ C3\alpha-H; \ W^2_2 = 18 \ Hz), \ 2.0 \ (s, \ CH_3COO), \ 1.1 \ (C1O-CH_3), \ 0.70 \ (C13-CH_3), \ 0.90 \ and \ 0.80 \ (other \ methyl \ protons). \]

Reaction of 3\beta-acetoxv-5,6\alpha-epoxv-5\alpha-cholestane (LXXXVII) with lead (IV) acetate : 3\beta-Acetoxycholest-5-ene (LVIII) and 3\beta,5-diacetoxv-6\beta-hydroxy-5\alpha-cholestane (XClII)

A mixture of 3\beta-acetoxv-5,6\alpha-epoxv-5\alpha-cholestane (LXXXVII) (2 g, 4.50 m mol), lead (IV) acetate (1.1 g, 2.24 m mol) and anhydrous potassium acetate (1 g) were refluxed in glacial acetic acid (150 ml) for 8 hrs. The mixture was cooled to room temperature, diluted with ice-cold water and extracted with ether. The ethereal solution was washed with sodium bicarbonate solution (5%) and water and dried over anhydrous sodium sulphate. Evapora-
tion of the solvent left a residue which was chromatographed over silica gel (40 g). Elution with light petroleum ether: ether (1:3) and with ether yielded 3β-acetoxycholest-5-ene (LVIII)\(^{37}\) (500 mg, 1.15 m mol) m.p. 116° and 3β,5-diacetoxy-6β-hydroxy-5α-cholestane (XCI) (480 mg, 9.60 m mol), m.p. 96°. The compounds (LVIII) and (XCI) were also obtained by the reaction of (LXXXVII) with lead (IV) acetate as described previously and were found to be identical in all respects to the authentic samples\(^{37}\).

3β,5-Dihydroxy-5α-cholestan-6-one oxime (XCIII)

3β,5-Dihydroxy-5α-cholestan-6-one (XCIII) (2.0 g), hydroxylamine hydrochloride (2.0 g) and sodium acetate (4.0 g) were taken in 80 ml of methanol and the reaction mixture was refluxed for 2 hrs on water bath. The progress of the reaction was monitored by TLC. After the complete conversion, the excess of the solvent was removed under reduced pressure and the residue was poured in to ice-cold water. Solid thus obtained was filtered, dried and recrystallized from methanol to give 3β,5-dihydroxy-5α-cholestan-6-one oxime (XCIII) (1.5 g), m.p. 235° (reported\(^{41}\) 227-229°).

3β-Chloro-5-hydroxy-5α-cholestan-6-one oxime (XCIV)

3β-Chloro-5-hydroxy-5α-cholestan-6-one (XCIV) (2.0 g) in ethanol (120 ml), hydroxylamine hydrochloride (5.0 g) and sodium
acetate trihydrate (8 g) were mixed together and the mixture was refluxed for 2 hrs. Excess of the solvent was removed under reduced pressure and the residue was diluted with ice-cold water. The crude oxime (XCIV) thus obtained was filtered and recrystallized from ethanol (1.6 g), (m.p. 190°) (reported39, 190°).

3β-Acetoxy-5-hydroxy-5α-cholestan-6-one oxime (XCV) :

3β-Acetoxy-5-hydroxy-5α-cholestan-6-one (XCV) (2.0 g), hydroxylamine hydrochloride (2.0 g) and sodium acetate (4.0 g) were taken in 80 ml of methanol and the reaction mixture was refluxed for 2 hrs on water bath. The progress of the reaction was monitored by TLC and after the complete conversion the excess solvent was removed under reduced pressure and the residue was poured into ice-cold water. Solid thus obtained was filtered dried and was recrystallized from methanol to give (XCV) (1.8 g) m.p. 146° (reported41, 146-150°).

Reaction of 3β,5-dihydroxy-5α-cholestan-6-one oxime (XCIII) with lead (IV) acetate in benzene and acetic acid : 3β-Acetoxycholestan-4-en-6-one (XCVI), 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (XCVIII) and 3β,5-dihydroxy-5α-cholestan-6-N-acyloxime (C)

Lead (IV) acetate (2.0 g, 4.48 m mol) was added in portions to a stirred solution of oxime (XCIII) (2.0 g, 4.62 m mol) in benzene (40 ml) and acetic acid (20 ml). The mixture was stirred at room temperature for 2 hrs. After the completion of the
reaction the solvent was removed under reduced pressure. The residue was taken up in ether and the ethereal extract was successively washed with water, sodium bicarbonate solution (5%) and again with the water and dried over anhydrous sodium sulphate. Removal of the solvent gave an oil (1.9 g) which was chromatographed over silica gel (40 g). Elution with light petroleum ether : ether (20:1) yielded a solid compound which was recrystallized from methanol to give (XCVI) (300 mg, 0.678 m mol) m.p. 107° (reported®, 106°).

Analysis Found : C, 78.67; H, 10.83
C_{29}H_{46}O_{3} requires : C, 78.60; H, 10.8%.

IR : \( \nu_{\text{max}} \) 1740 (CH_3COO), 1680 (C=O), 1625 (C=C), 1260 and 1040 cm\(^{-1}\) (C-O).

\(^{1}H\)-NMR : \( \delta \) 5.4 (brs, C4-vinylic H), 4.5(mc, C3a-H, \( J = 18 \) Hz), 2.0 (s, CH_{3}COO-), 1.1 (C10-CH_{3}), 0.75 (C13-CH_{3}), 0.90 and 0.80 (other methyl protons).

Further elution with petroleum ether : ether (10:1) furnished the compound (XCVIII) as a solid which was recrystallized from methanol-acetone mixture (250 mg, 0.550 m mol) m.p. 238° (reported®, 238°).

Analysis Found : C, 75.65; H, 10.51
C_{29}H_{48}O_{4} requires : C, 75.70; H, 10.50%.

IR : \( \nu_{\text{max}} \) 3400 (O-H), 1735 (CH_{3}COO-), 1680 (C=O), 1150 and 1020 cm\(^{-1}\) (C-O).
Continued elution with petroleum ether : ether (5:1) yielded (C) as semi-solid which was recrystallized from methanol (200 mg, 0.384 m mol) m.p. 176°.

Analysis Found : C, 71.94; H, 9.92; N, 2.74
C\textsubscript{29}H\textsubscript{49}O\textsubscript{4}N requires : C, 71.90; H, 9.90; N, 2.70%. IR : \(\delta\) max. 3350 (\(-\text{OH}\)), 1725 (CH\textsubscript{3}COO\textsuperscript{-}), 1680 (C=\text{N}), 1210 and 1050 cm\(^{-1}\) (C-\text{O}).

\(^1\text{H-NMR} : \delta 3.8 \text{ (mc, C3\alpha-H; } W^2 = 16 \text{ Hz), 2.15 (s, C5\alpha-\text{OH}), 1.9 (s, CH\textsubscript{3}COO\textsuperscript{-}), 1.20 (C10-CH\textsubscript{3}), 0.75 (C13-CH\textsubscript{3}), 0.95 and 0.85 (other methyl protons).}

Reaction of 3\beta-chloro-5-hydroxy-5\alpha-cholestan-6-one oxime (XCIV) with lead (IV) acetate in benzene and acetic acid : 3\beta-Chlorocholest-4-en-6-one (XCVII), 3\beta-chloro-7\alpha-acetoxyl-5-hydroxy-5\alpha-cholestan-6-one (XCIX) and 3\beta-chloro-5-hydroxy-5\alpha-cholestan-6-N-acyloxime (CI)

Lead (IV) acetate (2.0 g, 4.48 m mol) was added in portions to a stirred solution of oxime (XCIV) (2.0 g, 4.42 m mol) in dry benzene (40 ml) and acetic acid (20 ml). The mixture was stirred at room temperature for 2 hrs. After the completion of the reaction the solvent was removed under reduced pressure. The
residue was taken up in ether and the ethereal extract was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. The removal of the solvent gave an oil (1.5 g) which was chromatographed over silica gel (30 g). Elution with light petroleum ether : ether (16:1) yielded a solid compound which was recrystallized from acetone to give (XCVII) (250 mg, 0.610 m mol) m.p. 163° (reported^40, 163-165°) (positive Beilstein test).

Analysis Found : C, 74.16; H, 10.37
C_{27}H_{44}OCl requires : C, 74.20; H, 10.40%

IR : \( \nu_{\text{max.}} \) 1680 (C=O), 1625 (C=C) and 760 cm\(^{-1}\) (C-Cl).

\( ^1\text{H-NMR} : \delta 5.4 \text{ (brs, C4-vinylic-H), 3.8 (mc, C3a-H, } \frac{J}{2} = 16 \text{ Hz), 1.20 (C10-CH}_3 \text{), 0.70 (C13-CH}_3 \text{), 0.95 and 0.85 (other methyl protons)}.\)

Further elution with petroleum ether : ether (10:1) yielded the compound (XCIX) as solid which was recrystallized from petroleum ether (200 mg, 0.420 m mol) (positive Beilstein test), m.p. 87°.

Analysis Found : C, 70.35; H, 9.51
C_{29}H_{47}O_4Cl requires : C, 70.40; H, 9.60%

IR : \( \nu_{\text{max.}} \) 3500 (-OH), 1735 (CH\(_3\)COO-), 1690 (C=O), 1240, 1040 (C-O) and 750 cm\(^{-1}\) (C-Cl).

\( ^1\text{H-NMR} : \delta 4.7 \text{ (br, C7β-H, } \frac{J}{2} = 5 \text{ Hz), 3.4 (mc, } \frac{J}{2} = 16 \text{ Hz), 2.3 (s, C5α-CH}_3 \text{), 2.05 (s, CH}_3\text{COO-), 1.20 (C10-CH}_3 \text{), 0.70 (C13-CH}_3 \text{), 0.95 and 0.85 (other methyl protons)}.\)
Continued elution with light petroleum ether : ether (5:1) gave (Cl) as noncrystallizable oil (140 mg, 0.312 m mol).

Analysis Found: C, 70.51; H, 9.73; N, 2.89

C_{29}H_{48}O_3NCl, requires: C, 70.30; H, 9.60; N, 2.90%.

IR: ν_{max} 3450 (OH), 1745 (CH_3COO-), 1560 (C=N), 1240, 1020 (C-O) and 760 cm^{-1} (C-Cl).

^1H-NMR: δ 3.4 (mc, C3α-H; J = 18 Hz), 2.4 (s, C5α-OH), 2.0 (s, CH_3COO-), 1.20 (Cl0-CH_3), 0.70 (C13-CH_3), 0.95 and 0.85 (other methyl protons).

Reaction of 3β-acetoxv-5-hydroxy-5α-cholestan-6-one oxime (XCV) with lead (IV) acetate in benzene and acetic acid: 3β-Acetoxv-cholest-4-en-6-one (XCVI), 3β-acetoxv-5-hydroxy-5α-cholestan-6-one (XCVII) and 3β-acetoxv-5-hydroxy-5α-cholestan-6-N-acyloxime (CII)

Lead (IV) acetate (2.0 g, 4.48 m mol) was added in portions to a stirred solution of oxime (XCV) (2.0 g, 4.20 m mol) in dry benzene (40 ml) and acetic acid (20 ml). The mixture was stirred at room temperature for 2 hrs and the solvent was removed under reduced pressure. The residue thus obtained was worked up as described earlier and oil (1.3 g) obtained was chromatographed over silica gel (25 g). Elution with light petroleum ether : ether (20:1) and (10:1) afforded 3β-acetoxvcholest-4-en-6-one (XCVI) (250 mg, 0.565 m mol), m.p. 107° and 3β-acetoxv-5-hydroxy-5α-
cholestan-6-one (XCVIII) (200 mg, 0.440 m mol), m.p. 238\degree. The compound (XCVI) and (XCVIII) were found identical (m.p., m.m.p., IR and \(^1\)H-NMR) with the products obtained in the reaction of lead (IV) acetate with 3\beta,5-dihydroxy-5\alpha-cholestan-6-one oxime (XCIII).

Further elution with petroleum ether : ether (5:1) provided (CII) as an oil (200 mg, 0.480 m mol).

Analysis Found

\[
\begin{align*}
\text{C}_31\text{H}_51\text{O}_5\text{N} & \quad \text{requires} \\
\text{Analysis Found} & \quad \text{requires} \\
\text{C}, 72.61; \ H, 9.86; \ N, 2.71 & \quad \text{C}, 72.70; \ H, 9.9; \ N, 2.60\%.
\end{align*}
\]

IR

\[
\begin{align*}
\text{IR} & \quad \lambda_{\text{max}}. \ 3400 (-\text{OH}), 1735, 1715 (2 \times \text{CH}_3\text{COO}^-), 1660 (\text{C=N}), 1240 \text{ and } 1060 \text{ cm}^{-1} (\text{C-O}).
\end{align*}
\]

\(^1\)H-NMR

\[
\begin{align*}
\text{\(^1\)H-NMR} & \quad \delta 4.45 (\text{mc, } \text{C}3\alpha-\text{H}; \ \text{J} = 16 \text{ Hz}), \ 2.2 (\text{s, } \text{C}5\alpha-\text{OH}), \ 2.1,2.0 (\text{s, acetate protons}) 1.2(\text{CI}_0-\text{CH}_3), \ 0.75 (\text{CI}_3-\text{CH}_3), \ 0.95 \text{ and } 0.85 (\text{other methyl protons}).
\end{align*}
\]
References


Part Four

Solid Phase Syntheses:
Steroidal Reactions on
Alumina Surface
Alumina and silica gel being an adsorbent provide a reaction site for various interesting transformations. It also provides a reactive surface for the chromatographic conversion of alkylhalides into nitrates. The scope of surface reactions on alumina has further been diversified by G.H. Posner et al. by applying it to olefin forming elimination reactions, for example, reaction of 4,4-dimethylnósteryl-3-tosylate (I) on neutral alumina afforded diene (II).

\[ \text{TsO} \]
\[ \text{C}_{8}\text{H}_{17} \]
\[ \text{Al}_2\text{O}_3, \text{Et}_2\text{O} \]
\[ 25^\circ, 24 \text{ hrs} \]

(I)

Reich et al. performed the reaction of 3\(\beta\)-tolyloxy-5\(\alpha\)-hydroxycholestan-6-one (III) with dry alumina and reported the formation of \(\Delta^2\)-cholesten-5\(\alpha\)-ol-6-one (IV).
Peterson and Chen\textsuperscript{4} reported the reaction of cholest-4-en-7β-ol benzoate (V) on alumina column and obtained cholest-4-en-3-on -7β-ol benzoate (VI).

Douglas et al.\textsuperscript{5} reported the reaction of alumina in presence of methanol and potassium acetate with 3β-tosyloxy-5α-cholestane (VII) and the elimination of tosylate group was observed in the product (VIII).
Bernoulli et al.\textsuperscript{6} carried out the reaction of alumina in presence of acetic acid with cinobufotalon (IX) and obtained anhydrocinobufotalon (X) in 35\% yield.

Engel et al.\textsuperscript{7} reported the transformation of methyl $^{\triangle 4}$-3-oxo-12\alpha-tosyloxy-17\alpha-methylene-17\alpha-methyletienate (XI) with collidine and alumina into methyl $^{\triangle 4,\text{II}}$-3-oxo-17\alpha-methyletadienate (XII) whereas 12\alpha-mesyloxy pregnane-3,20-dione (XIII) when passed on to the alumina column afforded the $^{\triangle 11}$-pregnene-3,20-dione (XIV) as the product.\textsuperscript{8}
Schulz and Tamm\textsuperscript{9} reported the elimination of acetate moiety from 3\( \beta \),20\( \beta \)-diacetoxy-5\( \alpha \)-pregnan-1-one (XV) when it was passed through the alumina column and 20\( \beta \)-acetoxy-5\( \alpha \)-pregnan-2-en-1-one (XVI) as the product was obtained.
Henbest et al.\textsuperscript{10} during the reaction of $2\beta$-acetoxy-3-oxo-5\textalpha-cholestan e (XVII) with alumina obtained $2\alpha$-acetoxy-3-oxo-5\textalpha-cholestan e (XVIII) as the product while $2\alpha$-acetoxy-3-oxo-5\textalpha-cholestan e (XIX) gave $3\beta$-acetoxy-2-oxo-5\textalpha-cholestan e (XX).

\[
\begin{array}{c}
\text{AcO} \\
\text{C}_8\text{H}_{17}
\end{array}
\xrightarrow{\text{Al}_2\text{O}_3 \ 1 \ hr}
\begin{array}{c}
\text{AcO} \\
\text{C}_8\text{H}_{17}
\end{array}
\]

(XVII) \hspace{2cm} (XVIII)

\[
\begin{array}{c}
\text{AcO} \\
\text{C}_8\text{H}_{17}
\end{array}
\xrightarrow{\text{Al}_2\text{O}_3 \ 16 \ hrs}
\begin{array}{c}
\text{AcO}
\end{array}
\]

(XIX) \hspace{2cm} (XX)

Biggerstaff and Gallagher\textsuperscript{11} obtained (XXII) when the reaction was carried out on alumina surface with (XXI).
Rowland and Nace\textsuperscript{12} reported the reaction of \(3\beta\)-acetoxy-5,6\(\alpha\)-epoxy-5\(\alpha\)-cholestan (XXIII) with ethyl acetate washed alumina and \(3\beta\)-acetoxy-5,6\(\beta\)-dihydroxy-5\(\alpha\)-cholestan (XXIV) as the product was obtained.

Nambara and Fishman\textsuperscript{13} reported the reaction of \(3\beta,17\alpha\)-diacetoxy-16-oxido-5\(\alpha\)-14\(\beta\)-androstane (XXV) with acid washed alumina and obtained \(17\)-oxo-5\(\alpha\),14\(\beta\)-androstane-3\(\beta\),16\(\beta\)-diol diacetate (XXVI) and \(17\)-oxo-5\(\alpha\),14\(\beta\)-androstane-3\(\beta\)-acetoxy-16\(\beta\)-ol(XXVII).
Lyman et al.\textsuperscript{14} reported a convenient method for the addition of HI to unsaturated hydrocarbons (XXVIII and XXX) by using I\textsubscript{2} on alumina and they obtained (XXIX) and (XXXI) as the products.

Keinan and Mazur\textsuperscript{2} studied the reactions in dry medium. They passed 3β-acetoxycholest-4-ene (XXXII) over ferric chloride on silica gel and obtained cholesta-3,5-diene (XXXIII) in 90\% yield.
Nishiguchi et al.\textsuperscript{15} reported the dehydration of alcohols catalysed by copper (II) sulphate adsorbed on silica gel. The results were summarized in table - 1.

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Time (Min)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-MethyIcyclododecanol (XXXIX)</td>
<td>30</td>
<td>Methylenecyclododecane (XLIII)</td>
<td>(52)</td>
</tr>
<tr>
<td>Cyclododecanol (XLII)</td>
<td>15</td>
<td>1-MethyIcyclododecene (XLIII)</td>
<td>(46)</td>
</tr>
<tr>
<td>Cyclododecane (XXXVII)</td>
<td>40</td>
<td>Cyclododecene (XLIII)</td>
<td>(98)</td>
</tr>
</tbody>
</table>
Ferreira and coworkers\textsuperscript{16} reported the cleavage of carbon-carbon double bond (Table - II) by using solid supported potassium permanganate on silica gel.

**Table - II**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Product</th>
<th>Yield%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Methylcyclohexanol (Cis and trans mixture) (XLIV)</td>
<td>OH</td>
<td>60</td>
</tr>
<tr>
<td>4-Methylcyclohexanol (Cis and trans mixture) (XLVI)</td>
<td>OH</td>
<td>50</td>
</tr>
<tr>
<td>1-Phenylethanol (XLIX)</td>
<td>OH</td>
<td>50</td>
</tr>
<tr>
<td>1-Methylcyclohexene (XLV)</td>
<td></td>
<td>71</td>
</tr>
<tr>
<td>3-and 4-Methylcyclohexene (XLVII)</td>
<td></td>
<td>88</td>
</tr>
<tr>
<td>1-Methylcyclohexene (XLVIII)</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Styrene (L)</td>
<td></td>
<td>83</td>
</tr>
</tbody>
</table>

\[ \text{Ferreira and coworkers\textsuperscript{16} reported the cleavage of carbon-carbon double bond (Table - II) by using solid supported potassium permanganate on silica gel.} \]
Suarez and Mazzieri\textsuperscript{17} carried out the dehydrohalogenation of vicinal-dihaloalkanes (LXVIII), (LXX), (LXXIII) over silica gel and obtained (LXIX) (LXXI) (LXXII) and (LXXIV) as the products.
Sookim et al.\textsuperscript{18} carried out the efficient and selective cleavage of acetals and ketals by using ferric chloride adsorbed on silica gel and obtained hydroxy compounds and ketones (Table - III).

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
\textbf{Compound} & \textbf{Product} & \textbf{Time/hrs} & \textbf{Solvent} \\
\hline
(LXXV) & HO\text{OH} & 6 & CHCl\textsubscript{3} \\
(LXXVI) & HO\textsubscript{OH} & & CHCl\textsubscript{3} \\
(LXXVII) & & 8 & CHCl\textsubscript{3} \\
\hline
\end{tabular}
\caption{Table - III}
\end{table}
Corte and coworkers\textsuperscript{19} reported a convenient synthesis of ketene imine (XCI) by dehydrocyanation of imidoyl cyanides (XC) using vacuum gas solid reactions.

\[
\begin{align*}
R^1CH_2CHO + RCH_2NH_2HCl + NaCN & \xrightarrow{\text{MeOH-H}_2\text{O \text{r.t.}}} R'-CH_2-CH-NH-CH_2R \\
(\text{LXXXIX}) & \\
& \xrightarrow{t-BuOK, 110^\circ} R'-CH=\text{C}=\text{N}-\text{CH}_2R \\
(\text{XCI}) & \\
& \xrightarrow{110^\circ} R'-CH_2-C=\text{N}-\text{CH}_2R \\
(\text{XC})
\end{align*}
\]
Clark and coworkers\textsuperscript{20} carried out the synthesis of organofluorine compounds by using potassium fluoride-tetra-phenyl phosphonium bromide system and obtained (XXXV) as the product.

\[
\begin{align*}
\begin{array}{c}
\text{Cl} \\
\text{NO}_2 \\
\end{array} & \xrightarrow{\text{KF}} \\
\begin{array}{c}
\text{CF}_3 \\
\text{NO}_2 \\
\end{array} \\
\text{K(Ph}_4\text{P)Br} & \xrightarrow{\text{CH}_3\text{CN}} \\
\begin{array}{c}
\text{F} \\
\text{NO}_2 \\
\end{array}
\end{align*}
\]

(XCII)  (XCIII)
REACTION OF STEROIDAL NITROOLEFINS ON ALUMINA SURFACE

Basic alumina has been usefully employed for the preparation of dienoic esters from β-allenic esters in good yield with high stereospecificity\textsuperscript{21,22}. We report a simple method for the preparation of 6-nitrocholesta-3,5-diene, a versatile intermediate for the synthesis of steroidal compounds over alumina surface. 3β-Hydroxy-6-nitrocholest-5-ene (XCIV)\textsuperscript{23} its 3β-acetoxy (XCV)\textsuperscript{24} and 3β-tosyloxy (XCVI)\textsuperscript{25} analogues when allowed to stand over a column of basic alumina over night, formed 6-nitrocholesta-3,5-diene (XCVIII)\textsuperscript{26,26a} in quantitative yield.
Reaction of 3β-hydroxy-6-nitrocholest-5-ene (XCIV) on basic alumina : 6-Nitrocholesta-3,5-diene (XCVIII)

A solution of 3β-hydroxy-6-nitrocholest-5-ene (XCIV) dissolved in dry ether was adsorbed on basic alumina. The residual ether was removed under reduced pressure and the reaction mixture was kept at room temperature for 48 hrs. Elution with ether yielded a semi-solid on evaporation which on crystallization from methanol afforded a compound (XCVIII) m.p. 72°.

Identification of the compound, m.p. 72° as 6-nitrocholesta-3, 5-diene (XCVIII)

The compound, m.p. 72° was correctly analyzed for \( C_{27}H_{43}NO_2 \). The IR spectrum of the compound exhibited band at 1690 cm\(^{-1}\) for (-C=C= C-NO\(_2\)). The other characteristic bands were at 1515 and 1350 cm\(^{-1}\) (C-NO\(_2\)). The \(^1\)H-NMR spectrum exhibited a doublet at \( \delta 6.4 \) (\( J = 10\)Hz) for C4-proton and a
multiplet ascribed to C3-proton at δ 6.0. The methyl protons appeared at δ 1.28 (C10-CH3), 0.68 (C13-CH3), 0.92 and 0.80 (other methyl protons). On the basis of above facts the compound, m.p. 72° was identified as 6-nitrocholesta-3,5-diene (XCVIII). This compound was found identical with authentic sample of 6-nitrocholesta-3,5-diene (XCVIII). The 3β-acetoxy-6-nitrocholestat-5-ene (XCV) and 3β-tosyloxy-6-nitrocholesta-5-ene (XCVI) over alumina surface suffered the same type of elimination reaction and provided 6-nitrocholesta-3,5-diene (XCVIII) but 3β-chloro-6-nitrocholesta-5-ene (XCVII), failed to give (XCVIII), was eluted unreacted. As expected it has been observed that the elimination of tosloxy group in (XCVI) is faster as compared to acetoxy and hydroxyl groups in (XCV) and (XCVI), respectively.

**Scheme 1**

\[
\text{RO} \quad \xrightarrow{\text{Basic Al}_2\text{O}_3} \quad \text{N}^+ \quad \xrightarrow{\text{R}} \quad \text{NO}_2
\]

(XCVI) \quad Ts

(XCV) \quad Ac

(XCVI) \quad H

(XCVII) \quad (XCVII)

(XCVIII)
The reaction is under study to advance some reasons as to why the corresponding chloroderivative is refusing the similar elimination reactions. It is proposed to extend the study with compounds having other halo atoms at C3 and some oxygen containing functional groups at the same position. It is however worth speculative that oxygen attached to C3 may have some important role to play. This reaction however, provides a simple method for dehydration of alcohol to conjugated diene system attached to nitro group. The same compound (XCVIII) was prepared in our laboratory through other synthetic route26a.
REACTION OF STEROIDAL EPOXIDES ON SILVER NITRATE-ALUMINA SURFACE

A chromatographic column of silver nitrate alumina provides a reactive surface for a ready conversion of some olefins into corresponding alkyl nitrates. Better yield and time efficiency of this technique prompted us to use it for the transformation of steroidal epoxides to steroidal olefins.

5,6α-Epoxy-5α-cholestane (XCIX), 3β-hydroxy-5,6α-epoxy-5α-cholestane (C), 3β-acetoxy-5,6α-epoxy-5α-cholestane (CI), and 3β-chloro-5,6α-epoxy-5α-cholestane (CII) when kept on the column of silver nitrate alumina overnight provided cholest-5-ene (CIII), 3β-hydroxycholest-5-ene (XXXVIII), 3β-acetoxycholest-5-ene (CV) and 3β-chlorocholest-5-ene (CV) as products on elution with ether respectively.
Reaction of 5,6α-epoxy-5α-cholestane (XCIX) on alumina silver nitrate surface: Cholest-5-ene (CIII)

5,6α-Epoxo-5α-cholestane (XCIX) dissolved in dry ether was applied on the prepared column of neutral alumina silver nitrate and it was left overnight. Elution with ether yielded the compound, m.p. 94°.

\[
\text{C}_8\text{H}_{17} \quad \xrightarrow{\text{Al}_2\text{O}_3(\text{Neutral})} \quad \text{C}_6\text{H}_{12}
\]

Identification of the compound, m.p. 94° as cholest-5-ene (CIII)

The compound (CIII) m.p. 94° was analyzed correctly for C\text{27}H\text{46}. The IR spectrum of the compound exhibited the band at 1640 cm\text{−1} (C=C). In its \textsuperscript{1}H-NMR spectrum a multiplet appeared at δ 5.28 (J\textsubscript{1/2} = 6 Hz)\textsuperscript{33} integrating for one proton and was assigned to C6-vinylic proton. The angular and side chain methyl protons were observed at δ 1.17 (C10-CH\textsubscript{3}), 0.70 (C13-CH\textsubscript{3}), 0.94 and 0.84 (other methyl protons). These evidences confirmed the compound, m.p. 94° as cholest-5-ene, which was found identical (m.p., m.m.p., IR and \textsuperscript{1}H-NMR) with the authentic sample of cholest-5-ene\textsuperscript{31}. 
Reaction of 3β-hydroxy (C), 3β-acetoxy (CI) and 3β-chloro (CII)-5,6α-epoxy-5α-cholestanes on alumina silver nitrate surface: 3β-Hydroxy (XXXVIII), 3β-acetoxy (CIV) and 3β-chloro (CV) cholest-5-enes

The epoxides (C-CII) were dissolved in dry ether and were applied on the prepared column of neutral alumina silver nitrate and were left over night. Elution with ether yielded compounds m.p. 149°, 116° and 96°, respectively.

![Diagram of reaction]

Identification of the compound m.p. 149° as 3β-hydroxycholest-5-ene (XXXVIII)

The compound (XXXVIII) m.p. 149° was analyzed correctly for C_{27}H_{46}O. The IR spectrum of the compound exhibited strong bands at 3410 cm^{-1} for (-OH) and 1625 cm^{-1} (C=C). The ^1H-NMR
spectrum of the compound exhibited multiplet at $\delta$ 5.26 for C6-vinylic proton ($W_2^1 = 8$ Hz) and at $\delta$ 3.21 for C3α-H ($W_2^1 = 18$ Hz, axial).

The angular and side chain methyl protons were observed at $\delta$ 1.28 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.90 and 0.84. The above discussion confirmed the compound, m.p. 149° as 3β-hydroxycholester-5-ene (XXXVIII). The isolated compound was found identical (m.p., m.m.p., IR and $^1$H-NMR) with authentic sample of 3β-hydroxycholester-5-ene$^{29}$.

Identification of the compound, m.p. 116° as 3β-acetoxycholester-5-ene (CIV)

The compound (CIV) m.p. 116° was analyzed correctly for C$_{29}$H$_{48}$O$_2$. The IR spectrum of the compound exhibited bands at 1735 (CH$_3$COO-), 1625 (C=C), 1235 and 1050 cm$^{-1}$ (C=O). The $^1$H-NMR spectrum of the compound gave a broad singlet at $\delta$ 5.30 ($W_2^1 = 7$ Hz)$^{33}$ for C6-vinylic proton and a multiplet at $\delta$ 4.45 for C3α-H ($W_2^1 = 18$ Hz)$^{33}$ and the acetate methyl protons were observed at $\delta$ 2.0 as a singlet. Angular and side chain methyl protons were observed at $\delta$ 1.16 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.98 and 0.83.

In the light of above discussion the compound, m.p. 116° was identified as 3β-acetoxycholester-5-ene (CIV). The isolated compound was found identical (m.p., m.m.p., IR and $^1$H-NMR) with authentic sample of 3β-acetoxycholester-5-ene$^{29}$. 
Identification of the compound, m.p. 96° as 3β-chlorocholest-5-ene (CV)

The compound, m.p. 96° was analyzed correctly for C_{27}H_{45}Cl. The IR spectrum of the compound gave bands at 1625 cm^{-1} (C=C) and 764 cm^{-1} (C-Cl). The ^{1}H-NMR spectrum of the compound gave a broad singlet at δ 5.29 (W_{1/2} = 8 Hz)^{33} for C6-vinylic proton. The C3α-proton was observed at δ 3.58 as a multiplet (W_{1/2} = 20 Hz)^{33}. Angular and side chain methyl protons were observed at δ 1.15 (C10-CH_{3}), 0.70 (C13-CH_{3}), 0.90 and 0.80. On the basis of above facts the compound, m.p. 96° was identified as 3β-chlorocholest-5-ene (CV) which was found similar (m.p., m.m.p., IR and ^{1}H-NMR) to the authentic sample of 3β-chlorocholest-5-ene^{32} (CV).
Experimental

Reaction of 3β-hydroxy-6-nitrocholest-5-ene (XCV) on alumina surface: 6-Nitrocholest-3,5-diene (XCVIII)

A solution of 3β-hydroxy-6-nitrocholest-5-ene (1.0 g, 2.32 mmol) dissolved in dry ether (20 ml) was adsorbed over basic alumina (20 g). The residual ether was removed under reduced pressure and the reaction mixture was kept at room temperature for 48 hrs. Elution with ether yielded a semi-solid mass which on recrystallization from methanol afforded 6-nitrocholesta-3,5-diene (XCVIII) as yellowish crystals (900 g, 1.87 mmol) m.p. 72° (reported26,26a, m.p. 72-73°).

Analysis Found : C, 78.42; H, 10.21; N, 3.25

C27H43NO2 requires : C, 78.40; H, 10.20; N, 3.3%.

IR : $\nu_{\text{max}}$ 1690 (C=C=C=C-NO$_2$), 1515 and 1350 cm$^{-1}$(C6-NO$_2$).

$^1$H-NMR : $\delta$ 6.4 (d, C4-H, J = 10 Hz), 6.0 (mc, C3-H), 1.28 (C10-CH$_3$), 0.68 (C13-CH$_3$), 0.92 and 0.80 (other methyl protons).

Under similar reaction conditions (same amounts of nitro-olefins and basic alumina were used) 3β-acetoxy-6-nitrocholest-5-ene (XCVI) and 3β-tosyloxy-6-nitrocholest-5-ene (XCVII) afforded 6-nitrocholesta-3,5-diene(XCVIII) in 91% and 93% yields,
respectively, but 3β-chlorocholest-5-ene failed to give (XCVIII) and was recovered unreacted in quantitative yield.

**Reaction of 5,6α-epoxy-5α-cholestane (XCIX) on alumina silver nitrate: Cholest-5-ene (CIII)**

5,6α-Epoxy-5α-cholestane (XCIX) (2.0 g, 5.18 m mol) dissolved in dry ether was applied on the prepared column of neutral alumina silver nitrate (40 g; 10 g silver nitrate) and was left over night. Elution with ether yielded cholest-5-ene (CIII) recrystallized from acetone (1.8 g, 4.68 m mol) m.p. 94° (reported^3^, m.p. 91.5°C).

Analysis Found : C, 87.80; H, 12.20

C<sub>27</sub>H<sub>46</sub> requires : C, 87.80; H, 12.20%.

IR : v<sub>max</sub> 1640 cm<sup>-1</sup> (>C=C<sub>)</sub>

<sup>1</sup>H-NMR : δ 5.28 (mc, J<sub>1/2</sub> = 6 Hz, C6-vinylic proton), 1.17 (Cl0-CH<sub>3</sub>), 0.70 (Cl3-CH<sub>3</sub>), 0.94 and 0.84 (other methyl protons).

**Reaction of 3β-hydroxy-5,6α-epoxy-5α-cholestane (C) on alumina silver nitrate: 3β-Hydroxycholest-5-ene (XXXVIII)**

3β-Hydroxy-5,6α-epoxy-5α-cholestane (C) (2.0 g, 5.00 m mol) dissolved in dry ether was applied on the prepared column of neutral alumina silver nitrate (40 g alumina : 10 g silver nitrate) and was left overnight. Elution with ether yielded
3β-hydroxycholest-5-ene (XXXVIII) recrystallized from acetone (1.6 g, 4.16 m mol) m.p. 149° (reported\(^\text{31}\), m.p. 145.5°).

Analysis Found: C, 80.59; H, 11.44

C\(_{27}H_{46}O\) requires: C, 80.50; H, 11.4%.

IR: \(\nu_{\text{max.}} 3410 \text{ (OH)}\) and 1625 cm\(^{-1}\) (C=O).

\(^1\text{H-NMR:} \delta 5.26 \text{ (mc, } \frac{\omega}{2} = 8 \text{ Hz, C6-vinyllic proton), 3.21 \text{ (mc, C3α-H; } \frac{\omega}{2} = 18 \text{ Hz), 1.28 (C10-CH}_3\text{), 0.68 (C13-CH}_3\text{), 0.90 and 0.84 (other methyl protons).}

**Reaction of 3β-acetoxy-5,6α-epoxy-5α-cholestane (CI) on alumina silver nitrate: 3β-Acetoxycholest-5-ene (CIV)**

3β-Acetoxy-5,6α-epoxy-5α-cholestane (CI) (2.0 g, 4.50 m mol) dissolved in dry ether was applied on the prepared column of neutral alumina silver nitrate (40 g, alumina: 10 g silver nitrate) and was left overnight at room temperature. Elution with ether yielded 3β-acetoxycholest-5-ene (CIV) recrystallized from acetone (1.65 g, 3.24 m mol) m.p. 116° (reported\(^\text{31}\), m.p. 116°).

Analysis Found: C, 81.31; H, 11.21

C\(_{29}H_{48}O_2\) requires: C, 81.30; H, 11.20%.

IR: \(\nu_{\text{max.}} 1735 \text{ (CH}_3\text{COO-)}, 1625 \text{ (C=O), 1235 and 1050 cm}^{-1} \text{ (C-O).}\)
$^1$H-NMR : δ 5.30 (brs, C6-vinylic proton), 4.45 (mc, C3α-H; $\omega_2^1 = 18$ Hz), 2.0 (s, CH$_3$COO$^-$), 1.16 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.98 and 0.83 (other methyl protons).

Reaction of 3β-chloro-5,6α-epoxy-5α-cholestane (CII) on alumina silver nitrate : 3β-Chlorocholest-5-ene (CV).

3β-Chloro-5,6α-epoxy-5α-cholestane (CII) (2.0 g, 4.96 m mol) dissolved in dry ether was applied on the prepared column of neutral alumina silver nitrate (40 g alumina : 10 g silver nitrate) and was left overnight at room temperature. Elution with ether yielded 3β-chlorocholest-5-ene (CV) recrystallized from acetone (1.92 g, 4.57 m mol) m.p. 96° (reported$^{34}$, 96-97°).

Analysis Found : C, 80.09; H, 11.12
C$_{27}$H$_{45}$Cl requires : C, 80.00; H, 11.1%.

IR : $\nu_{\text{max.}}$ 1625 (C=C) and 764 cm$^{-1}$ (C-Cl).

$^1$H-NMR : δ 5.29 (brs, C6-vinylic proton), 3.58 (mc, C3α-H; $\omega_2^1 = 20$ Hz), 1.15 (C10-CH$_3$), 0.70 (C13-CH$_3$), 0.90 and 0.80 (other methyl protons).
References


