CHAPTER FOUR

Synthesis of steroidal tetrazoles
THEORETICAL
The five membered doubly unsaturated heterocycle with one carbon and four nitrogen atoms is known as tetrazole. The first tetrazole was recognised in 1885 by Bladin during an investigation of dicyanophenylhydrazine. An excellent review covering methods of synthesis of tetrazoles and almost all aspects of tetrazole chemistry, is given by Benson.\(^1\)

Tetrazoles have important biological as well as non-biological applications. These have been applied in various explosives and in propellants. Nitrocellulose propellant powder is rendered flashless without loss of ballistic potential by incorporation of 5-aminotetrazole (I). They have also been used as binders in composite propellants and match compositions. They are of use in fibre, dye-stuff and textile industries and have application in photography too. It is also used in the shock treatment of certain psychosis to produce convulsions. Such convulsive effects produced by tetrazoles are of significant importance, as they are used as bird management chemical. The best known biologically active tetrazole is pentamethylenetetrazole (III), which is used in clinics to overcome intoxications owing to over dosage of barbiturates.\(^3\) Stimulant, depressant, sedative and analgesic activities are shown by certain tetrazoles. Anticonvulsant, hypertensive and adrenergic blocking actions are also exhibited by a number of 5-monosubstituted tetrazoles.\(^2\)
The synthesis of tetrazoles may be carried out by various methods like (i) oxidative ring closure, (ii) hydrazineazide reaction, (iii) rearrangements, (iv) acylhydrazine diazonium reaction, (v) addition of hydrazoic acid to compounds having carbon-nitrogen unsaturation, such as nitriles, cyanates, isothiocyanates and cyanamides, and (vi) hydrazine nitrite reaction. One of the most valuable method for preparation of tetrazole is the rearrangement reaction between ketones and an excess of hydrazoic acid in presence of strong acids as catalyst, a modification of the Schmidt-reaction.4,5

The reaction has found its most extensive applications with cyclic ketones, with which yields are generally better than with acyclic ketones. Champman et al.6 obtained pentamethylenetetrazole (III) from cyclohexanone (II). Benson2 synthesized the same tetrazole (III) from cyclohexanoneoxime (IV).
A probable mechanism for this transformation was given by Smith, in which the first step was the conversion of the compound to a carbonium ion under the influence of acid catalyst. This was followed by combination with one molecule of hydrazoic acid, dehydration of the intermediate and rearrangement to an imido-carbonium ion with a simultaneous loss of nitrogen. The formation of tetrazole took place with a reaction of second molecule of hydrazoic acid and imidocarbonium ion, the positive charge being lost as a proton. But instead of tetrazole a lactam was obtained if water molecule reacted with the imidocarbonium ion in place of a second molecule of hydrazoic acid. The mechanism accounted satisfactorily for the necessity of using strong acid as catalyst.
When a mixture of 2-methylpropanal (V), trimethylsilyl azide (3 equiv.) and zinc chloride (1 equiv.) was stirred at room temperature, yielded 1-(1-methylethyl)-1H-tetrazole (VI) and 5-(1-hydroxy-2-methylpropyl)-1-(1-methylethyl)-tetrazole (VII).^8

\[
\text{CH}_3 \text{-CH-CHO} + (\text{CH}_3)_3 \text{SiN}_3 \xrightarrow{\text{ZnCl}_2} \text{CH}_3 \text{-N-CH-CH}_3 \\
(\text{V})
\]

The reaction of sodium azide on the oximes of methyl oleanonate (VIII) and methyl betulonate (IX) in methylene-dichloride in presence of chlorosulphonic acid furnished 4-aza-A-homo-olean-28(13) lactone [3,4-d] tetrazole (X) and 4-aza-A-homo-28-oxoallobetulin [3,4-d] tetrazole (XI).^9

(VIII) (X)
Haughton et al.\textsuperscript{10} prepared 1,5-diaryltetrazole (XIII) by the reaction of imidoyl chlorides (XII) with sodium azide in N,N-dimethylformamide.

\[
\begin{align*}
&\text{Cl} \\
&\text{R}_1 \quad \text{R}_2 \quad \text{R}_3 \quad \text{R}_4
\end{align*}
\]

(XII)

Methyl-5-(acetylamino)-3,5-didesoxy-\(\beta\) - \(\Delta\) -glycero-D-galacto-2-nonulo-pyranosidonic methyl ester (XIV)\textsuperscript{11} was transformed into the corresponding amides (XV, XVI), the peracetylated (XV, XVI) were converted with POCl\(_3\) into the nitrile derivative (XVII) which on reaction with ammonium azide furnished (XVIII, XIX) with a bioisosteric tetrazole function.
Chnarakov et al.\textsuperscript{12} prepared the sodium salt of 1-oxy-5-cyanotetrazole (XXI) from aminoazidofurazane (XX).

Hassner et al.\textsuperscript{13} reported one of the most valuable method for the preparation of 1,5-disubstituted tetrazoles. In which a carbon carbon double bond was made to react with halogen and sodium azide using nitriles as solvent and proposed the following mechanism for the formation of tetrazole.
Steroidal tetrazoles

The first example of the formation of a tetrazole in steroid and triterpenoid was given by Barnes et al.\textsuperscript{14} in 1952. Treatment of 3β-acetoxy-7,11, dioxolanost-8-ene (XXII), with hydrazoic acid gave two isomeric monolactams (XXIII, XXIV), and a tetrazole, which was considered to be formed by the reaction with 7-oxo-function, having the structure (XXV) or (XXVI). The structure of the tetrazole could not be established very accurately.
Steroidal tetrazoles did not attract the attention of synthetic organic chemists until 1968, when Mechoulam\textsuperscript{15} reported the synthesis of a number of ring A fused steroidal tetrazoles and claimed that some of them possessed antifertility and antispermatic activities. From the Schmidt reaction of $5\alpha$-cholestan-3-one (XXVII) and $17\beta$-hydroxy-$5\alpha$-androstane-3-one (XXVIII) using excess of hydrazoic acid, Mechoulam obtained mixtures of isomeric tetrazoles (XXIX, XXXI and XXX, XXXII), respectively.

Similar treatment of 20,20-ethylenedioxy-$5\alpha$-pregnan-3-one (XXXIII) afforded a mixture of $17\beta$-(5-methyltetrazine-1-yl) 3-aza-$\Lambda$-homo-$5\alpha$-androstano [3,4-d] tetrazole (XXXIV) and its 4-aza, isomer (XXXV).\textsuperscript{15}
In 1970, Moural and Syhora\textsuperscript{16} reported the synthesis of a series of 3-aza-A-homo-4a-eno [3,4-d] tetrazole analogues from the corresponding 3-oxo-4-eno steroids by the reactions of hydrazoic acid. The reaction of 3-oxoandrost-4-en-17β-propionate (XXXVI) has been reported to yield tetrazole (XXXVIII) which on hydrogenation gave the corresponding dihydro derivatives (XXXIX). A tetrazole (XXXVIII) was also obtained when 3β-hydroximinoandrost-4-en-17β-propionate (XXXVII) was treated with hydrazoic acid. Similarly, 3-oxocholest-4-ene (XL) yielded 3-aza-A-homocholest-4a-eno [3,4-d] tetrazole (XLI).
Singh et al.\textsuperscript{17} obtained 3-aza-A-homo-(25R)-spirost-4a-eno [3,4-d] tetrazole (XLIII) in preference to the isomer (XLIV) on treating (25R)-siprost-4-en-3-one (XLII) with hydrazoic acid in the presence of BF\textsubscript{3}-etherate as catalyst. The structure (XLIII) was confirmed on the basis of spectral data. The observation was that, the Schmidt reaction of 4-en-3-one or the Beckmann rearrangement of the corresponding oxime generally afforded lactam, with 3-aza-A-homo-4a-eno-one system, which also supported the structure (XLIII) in preference to (XLIV). Marker's degradation of the tetrazole (XLIII) gave 3-aza-A-homopregna-4a,16-dieno [3,4-d] tetrazole-20-one (XLV).
Singh et al.\textsuperscript{18,19} have reported the reaction of androst-4-ene-3,17-dione (XLVI) with hydrazoic acid and BF$_3$-etherate in chloroform to get the expected 3,17a-diaza-A,D-bishomoandrost-4a-eno [3,4-d:17a, 17-d] bistetrazole (XLVII) and an unusual product 13,17-seco-13-azido-A-homoandrost-4a-eno [3,4-d] tetrazole-17-nitrile (XLVIII). The azidonitrile (XLVIII) cyclizes on heating to (XLVII). The structures were unequivocally established on spectral evidences. The example is claimed to be the first of its kind for the formation of azidonitrile in Schmidt reaction and its thermal cyclization to a tetrazole.

It has been reported by Singh and Paul\textsuperscript{20} that the treatment of 17a-methyl-17a-aza-D-homoandrost-4-en-3-one (XLIX) with an excess of hydrazoic acid in the presence of BF$_3$-etherate afforded 17a-methyl-3, 17a-diaza-A,D-bishomoandrostat-4a-eno [3,4-d] tetrazole (L).
Singh et al.\textsuperscript{21} have reported the synthesis of tetrazole from reaction of progesterone with hydrazoic acid and BF$_3$-etherate. Progesterone (LI) was shown to afford 17$\beta$-acetamido-3-aza-A-homoandrost-4a-eno [3,4-d] tetrazole (LII) and 17$\beta$ (5'-methyl-tetrazol-1'-yl) 3-aza-A-homoandrost-4a-eno [3,4-d] tetrazole (LIII). The structure (LII) was further confirmed when the same was obtained by the reaction of 17$\beta$-acetamidoandrost-4-en-3-one (LIV) with hydrazoic acid and BF$_3$-etherate.
The reactions of 6β-bromocholesta-4,6-dien-3-one (LV), 6-acetoxycholesta-4,6-dien-3-one (LVI) and 6-ethoxycholesta-4,6-dien-3-one (LIX) with an excess of hydrazoic acid in the presence of BF₃-etherate were also studied. The reaction of (LV) provided exclusively 3-aza-A-homocholesta-4a,6-dieno[3,4-d]tetrazole (LVII). Under similar reaction conditions, (LVI) furnished 6-acetoxy-3-aza-A-homocholesta-4a,6-dieno[3,4-d]tetrazole (LVIII) and (LIX) provided (LX), (LXI) and (LXII).

Reaction of 4-methylcholesta-4,6-dien-3-one (LXIII) with an excess of hydrazoic acid provided 3-aza-A-homo-4a-methyl-
cholest-4a-en-4-one (LXV) and 3-aza-A-homo-4a-methylcholest-4a-eno-\([3,4-d]\) tetrazole (LXVI). 4-Ethylcholest-4-en-3-one (LXIV) afforded 3-aza-A-homo-4a-ethylcholest-4a-eno \([3,4-d]\) tetrazole (LXVII) and its 4-aza isomer (LXVIII). Under similar reaction conditions 4,4-dimethylcholest-5-en-3-one (LXIX) provided 4,4-dimethyl-5\(^{-}\)-cholestane-3,6-dione (LXXI) and 4-aza-A-homo-4a,4a-dimethylcholest-5-eno \([4,3-d]\) tetrazole (LXXII). Where as, the 4,4-diethylcholest-5-en-3-one (LXX) furnished 4-aza-A-homo-4a,4a-diethylcholest-5-eno \([4,3-d]\) tetrazole (LXXIII) and 4,4-diethyl-3,4-seco-4\(^{\beta}\)-azidocholest-5-en-3-nitrile (LXXIV)."
A number of tetrazoles have been reported possessing the 6-aza-B-homo-5 Neh-cholestan-6-ones. Under the usual reaction conditions 5-cholestan-6-one (LXXV), its 3β-acetoxy (LXXVI), 3β-hydroxy (LXXVII) and 3β-chloro (LXXVIII) analogues furnished the corresponding tetrazoles (LXXIX-LXXXII) and the lactams (LXXXIII-LXXXVI). Similar types of ketones (LXXXVII-XVC) in stigmastane series also furnished the corresponding tetrazoles (XCVI-CIV). 26
The reaction of 5-bromo-5α-cholestan-6-one (CV) and its 3β-acetoxy analogue (CVI) with hydrazoic acid afforded the corresponding tetrazoles, 6-aza-5-bromo-B-homo-5α-cholestan-6,7-d] tetrazole (CVII), its 3β-acetoxy (CVIII) and 3β-hydroxy (CIX) analogues. Dehydrobromination of these tetrazoles (CVII-CIX) afforded 6-aza-B-homocholest-4-eno-6,7-d] tetrazole (CX), its 3β-acetoxy (CXI) and 3β-hydroxy (CXII) analogues. Jones oxidation of (CXII) gave 6-aza-3-oxo-B-homocholest-4-eno-6,7-d] tetrazole (CXIII).27
The reaction of 7a-aza-B-homocholest-4-eno [7a,7-d] tetrazole-3-one (CXIV) with equimolar quantity of sodium azide in polyphosphoric acid gave 4,7a-aza-A,B-bishomocholest-4a-eno [7a,7-d] tetrazole-3-one (CXV). With an excess of hydrazoic acid, (CXIV) provided a bistetrazole which could be either 3,7a-diaza-A,B-bishomocholest-4a-eno [3,4-d:7a,7-d] bistetrazole (CXVI) or its $\Delta^5$ isomer (CXVII).²⁸
Reaction of (25R)-7-oxospirost-5-en-3β-yl acetate (CXVIII) with hydrazoic acid afforded the corresponding tetrazole (CXIX). Marker's degradation followed by selective hydrogenation of (CXIX) yielded 20-oxo-7a-aza-B-homopregna-5,16-dieno [7a,7-d] tetrazole-3β-yl acetate (CXX). The tetrazole (CXX) on hydrolysis followed by oppenauer oxidation afforded 7a-aza-B-homopregen-4-eno [7a,7-d] tetrazole-3,20-dione (CXXIV). The treatment of 7-oxoandrost-5-en-3β,17β-diol diacetate (CXXI) with hydrazoic acid afforded 7a-aza-B-homoandrost-5-eno [7a,7-d] tetrazole-3β,17β-diol diacetate (CXXII). This tetrazole (CXXII) afforded 3-oxo-7a-aza-B-homoandrost-4-eno [7a,7-d] tetrazole-17β-yl acetate (CXXIII) on hydrolysis followed by oppenauer oxidation.29
Singh et al.\textsuperscript{30} reported the formation of 3-methoxy-17a-aza-D-homo-1,3,5(10)-estratrien-17a,17-d] tetrazole (CXXVI) and 3-methoxy 13,17-seco-13\textsubscript{a}-azido-1,3,5(10)-estratrien-17-nitrile (CXXVII) from estrone methyl ether (CXXV) using an excess of hydrazoic acid. The azido nitrile (CXXVII) on thermal cyclization provided tetrazole (CXXVI).

Cervantes et al.\textsuperscript{31} reported the formation of ring D fused tetrazoles from the reaction of 17-ketoximes with an excess of sodium azide in the presence of sulphuric acid. The reaction of 5\textsubscript{a}-androstan-17-one oxime (CXXVIII) was shown to afford 17a-aza-D-homo-5\textsubscript{a}-androstan-17\textsubscript{a},17\textsubscript{d}] tetrazole (CXXX) and D-homo lactam (CXXXIII). Similarly the oxime (CXXIX) furnished 3\beta-acetoxy-17a-aza-D-homo-5\textsubscript{a}-androstan-17\textsubscript{a},17\textsubscript{d}] tetrazole (CXXXI), its 3\beta-hydroxy analogue (CXXXII) and the lactam (CXXXIV). Similarly the oxime (CXXXV) yielded 17a-aza-3-hydroxy-D-homoestra-1,3,5(10)-triene [17a,
17-d] tetrazole-3-methyl ether (CXXXVI) along with the lactam (CXXXVII) and seconitrile (CXXXVIII).

When 5-\text{-}cyanocholest-3-en-6-one (CXXXIX) and 3,5-dicyano-5-\text{-}cholest-3-en-6-one (CXL) were treated with an excess of hydrazoic acid and BF$_3$-etherate (as catalyst)
afforded 5 \( \sim \) -cyano-6-aza-B-homocholest-3-eno [6,7-d] tetrazole (CXL) and 3,5-dicyano-6-aza-B-homocholest-3-eno [6,7-d] tetrazole (CXLII) respectively.\(^{32}\)

![Chemical structure of CXXXIX](image1)

![Chemical structure of CXLI](image2)

![Chemical structure of CXL](image3)

![Chemical structure of CXLII](image4)

Synthesis of bromo tetrazoles (CXLVI-CXLVIII) by the reaction of respective \( \sim \)-bromo ketones (CXLIII-CXLV) with hydrazoic acid in presence of BF\(_3\)-etherate was also reported.\(^{33}\)
R
(CXLIII) H
(CXLIV) Cl
(CXLV) OAc

\[ \text{(CXLVI)} \quad \text{H} \]
\[ \text{(CXLVII)} \quad \text{Cl} \]
\[ \text{(CXLVIII)} \quad \text{OAc} \]
Steroidal tetrazoles became of interest in recent past, because of the discovery of various biological activities such as hypertensive\(^2\), anticonvulsant\(^2,34\), antiallergic\(^35\), antiulcer\(^36\), antibacterial\(^37\), antiviral\(^37\), antifungal\(^37\) and analgesic\(^38\), associated with a number of substituted tetrazoles. As a result of this realization, synthesis of steroidal tetrazoles became a matter of interest and consequently a number of papers appeared describing the preparation of steroidal tetrazoles from various steroidal ketones.

The present work describes the preparation of \(\alpha\)-bromotetrazoles (CLII-CLIV) along with \(\alpha\)-bromoamides (CLV-CLVII) from the steroidal olefins such as cholest-5-ene (CXLIX), \(3\beta\)-chlorochest-5-ene (CL) and \(3\beta\)-acetoxy cholest-5-ene (CLI) and also the preparation of \(\alpha\)-hydroxy tetrazoles (CLXI-CLXIII), from the respective steroidal oxiranes (CLVIII-CLX).
REACTIONS OF STEROIDAL OLEFIN WITH BROMINE, ACETONITRILE AND SODIUM AZIDE

Reaction of cholest-5-ene (CXLIX) with bromine, acetonitrile and sodium azide in the presence of anhydrous aluminium chloride

Cholest-5-ene (CXLIX) in acetonitrile, was treated with bromine and sodium azide in the presence of anhydrous aluminium chloride. The suspension was stirred at 0°C and room temperature for 2 hrs each. The progress of the reaction was monitored by TLC. The solvent was removed and the residue was extracted with chloroform. The organic layer was washed with water, sodium bicarbonate solution and again with water and dried over anhydrous sodium sulphate. The removal of solvent provided an oily residue, which was chromatographed over silica gel to furnish two compounds, having m.p.s. 156°C and 172°C.
Characterization of the compound having m.p. 172°C as 5-bromo-6β-acetamido-5α-cholestane (CLV)

The compound with m.p. 172°C was correctly analysed for C_{29}H_{50}NOBr (positive Beilstein test). Its IR spectrum gave bands at 3420 (NH), 1670 (-CO-NH) and 730 cm^{-1} (C-Br). The ^1H-NMR spectrum of the compound exhibited a broad singlet centered at δ 5.8 integrating for one proton (deuterium exchangeable) and was assigned to N-H proton. A multiplet centered at δ 3.2 integrating for one proton was assigned to C6-α H. A sharp singlet integrating for three protons appeared at δ 2.1 due to methyl group of the amide moiety. Other methyl protons appeared at δ 1.2 (C10-CH₃), 0.72 (C13-CH₃), 0.97 and 0.84 (other side chain methyl protons). In the light of above observations, the compound having m.p. 172°C may therefore be regarded as 5-bromo-6β-acetamido-5α-cholestane (CLV). The mass spectral studies further supported the above structure for the compound (CLV). The mass spectrum of (CLV) gave the molecular ion peaks at m/z
507/509 (M⁺) followed by other significant peaks at m/z 492/494, 449/451, 448/450, 427; 394/396, 385, 368, and lower mass fragment ion peaks. Formation of some significant fragment ions has been explained in scheme which is tentative in nature.

Scheme

Characterization of the compound having m.p. 156°C as 5-bromo-5α-cholest-6β(1')-5'-methyltetrazole (CLII)

The compound (CLII) with m.p. 156°C was analyzed correctly for C₂₉H₄₉N₄Br. The IR spectrum of the compound exhibited bands at 1530, 1460, 1380 (C=N and N=N) and 740 cm⁻¹ (C-Br). The ¹H-NMR spectrum of the compound exhibited a broad signal centered at δ 3.1 integrating for one proton and was assigned to C6-αH. A sharp singlet appeared at δ 2.5 integrating for three protons, was assigned to 5'-methyl protons of tetrazole moiety. Other methyl protons appeared at
1.02 (Cl0-CH3), 0.7 (Cl3-CH3), 0.96 and 0.81 (other side chain methyl protons). These observations suggested the compound to be 5-bromo-5α-cholest-6β (1')-5'-methyltetrazole \((\text{CLII})\). This structure was further supported by mass spectral studies. The mass spectrum of (CLII) gave the molecular ion peak at m/z 532/534 (M+) followed by other significant peaks at m/z 517/519, 452, 449/451, 448/450, 419/421, 368, and lower mass fragment ion peaks. Formation of some of the significant fragment ions have been rationalized in scheme.

Reaction of 3β-chlorocholest-5-ene (CL) with bromine, acetonitrile and sodium azide in presence of anhydrous aluminium chloride

3β-Chlorocholest-5-ene (CL) in acetonitrile, was treated with bromine and sodium azide in presence of
anhydrous aluminium chloride. The suspension was stirred and worked up as described earlier. After column chromatography two oily compounds were obtained.

Characterization of the oily compound (CLVI) as 3β-chloro-5-bromo-6β-acetamido-5α-cholestane

The elemental analysis of the oily compound (CLVI) corresponded to the molecular formula C_{29}H_{49}NOBrCl (positive Beilstein test). The IR spectrum of the compound exhibited bands at 3410 (NH), 1660 (-NH-CO-), 740 and 715 cm\(^{-1}\) (C-Cl and C-Br). The \(^1\)H-NMR spectrum of the compound exhibited a broad singlet for one proton at \(\delta\) 5.8 which was assigned to the NH proton (deuterium exchangeable). Two multiplets centered at \(\delta\) 4.41 and 3.76 integrating for one proton each, were assigned to C\(_3\)-\(\alpha\)H (\(W\ 1/2 = 16 \text{ Hz, axial}\))\(^{39}\) and C\(_6\)-\(\alpha\)H (\(W\ 1/2 = 4.5 \text{ Hz, equatorial}\))\(^{38}\) respectively. A sharp singlet for three protons appeared at \(\delta\) 2.01 which was assigned to NH-CO-CH\(_3\). Other methyl protons were observed at \(\delta\) 1.26 (C10-CH\(_3\)), 0.68 (C13-CH\(_3\)), 0.95 and 0.82 (other side chain methyl protons). These values suggested the compound to be 3β-chloro-5-β-bromo-6β-acetamido-5α-cholestane (CLVI). This
structure was further supported by its mass spectral studies. In the mass spectrum of (CLVI), molecular ion peak appeared at m/z 541/543/545 (M+) followed by some other prominent fragment ions at m/z 526/528/530, 505/507, 483/485/487, 461/463, 447/449, 429/431, 428/430/432, 425, 393, 366 and were rationalized in scheme.

Characterization of the second oily compound as 3β-3-chloro-5-bromo-5-<cholest-6β(1')-5'-methyltetrazole (CLIII)

The oily compound (CLIII) was analyzed for C29H48N4BrCl (positive Beilstein test). The IR spectrum of the compound showed bands at 1525, 1460, 1375 (C=N and N=N) 16,17, 740 and 720 cm⁻¹ (C-Cl, and C-Br). The 1H-NMR spectrum of the compound exhibited a multiplet at δ 3.95 for one proton and was assigned to C3-<H (W 1/2 = 16 Hz, axial). Another
A multiplet for one proton appeared at 3.6 which was assigned to C6-< H (W 1/2 = 4 Hz, equatorial). A sharp singlet integrating for three methyl protons of tetrazole moiety appeared at δ 2.52. Other methyl protons appeared at δ 1.2 (C10-CH₃), 0.7 (C13-CH₃), 0.91 and 0.80 (other side chain methyl protons). The mass spectrum of the compound showed signals at m/z 566/568/570 (M⁺), 551/553/555, 530/532, 453/455/457, 450, 446/448, 402/404 and 366 as given in scheme. On the basis of above analytical and spectral data, the oily compound was characterized as 3β-chloro-5-bromo-5α-cholest-6β (1')-5'-methyltetrazole (CLIII).
Reaction of 3β-acetoxy cholest-5-ene (CLI) with bromine, acetonitrile and sodium azide in presence of anhydrous aluminium chloride

3β - Acetoxycholest-5-ene (CLI) was dissolved in acetonitrile, and was treated with bromine, sodium azide in presence of anhydrous aluminium chloride. After the completion of the reaction, the reaction mixture was worked up as usual and the solvent was removed. The crude product thus obtained was chromatographed over silica gel affording two products having m.ps. 159°C and 178°C.

Characterization of the compound having m.p. 159°C as 5-bromo-6β-acetamido-5α-cholest-3-ene (CLVII).

The elemental analysis of the compound with m.p. 159°C corresponded to the molecular formula C_{29}H_{48}NOBr (positive Beilstein test). Its IR spectrum exhibited bands at 3430 (NH), 1670 (−NH−CO−), 1625 (C=C), and 730 cm−1 (C−Br). The $^1$H-NMR spectrum of the compound displayed a broad singlet centered at δ 6.2 (deuterium exchangeable) for one proton and was assigned to NH proton. A broad multiplet for two protons
appeared at 6 5.5-5.4 due to C3 and C4 vinylic protons. A signal at 6 3.2 for one proton was found for C6-<H (W1/2 = 5Hz, equatorial). A sharp singlet for the methyl protons of the amide moiety appeared at 6 2.1. Other methyl protons were observed at 6 1.2 (C10-CH₃), 0.7 (C13-CH₃), 0.97 and 0.83 (other side chain methyl protons). The mass spectrum of the compound gave molecular ion peak at m/z 505/507 (M⁺) and some prominent ion peaks at m/z 490/492, 447/449, 446/448, 425, 392/394, 382 and 366 as rationalized in scheme. On the basis of these values, the compound with m.p. 159°C was characterized as 5-bromo-6β-acetamido-5<cholest-3-ene (CLVII).

Characterization of the compound with m.p. 178°C as 5-bromo-5<cholest-3-en-6β (1')-5'-methyltetrazole (CLIV).

The compound having m.p. 178°C showed the molecular composition C₂₉H₄₇N₄Br. The IR spectrum of the compound
exhibited bands at 1520, 1465, 1380 (C=N and N=N) \(16,17\), 1620 (C=C) and 730 cm\(^{-1}\) (C-Br). The \(^1\)H-NMR spectrum of the compound displayed a broad multiplet at \(\delta\) 5.53-5.45 integrating for two protons and was assigned to C3 and C4 vinylic protons. A multiplet centered at \(\delta\) 3.06 for one proton was assigned to C6-\(\langle\)H (\(\text{W}_{1/2} = 4.5\) Hz, equatorial).\(^3\) The methyl protons of tetrazole moiety appeared at \(\delta\) 2.56. Other methyl protons were observed at \(\delta\) 1.15 (Cl0-CH\(_3\)), 0.71 (Cl3-CH\(_3\)), 0.92 and 0.80 (other side chain methyl protons). In the mass spectrum the molecular ion peak observed at m/z 530/532 (\(M^+\)) and other prominent ion peaks were appeared at m/z 515/517, 447/449, 446/448, 450, 417/419 and 366 as given in scheme. On the basis of these data, the compound having m.p. 178°C was characterized as 5-bromo-5'-cholest-3-en-6β (1')-5'-methyltetrazole (CLIV).

\textbf{Scheme}

\[\text{Scheme diagram with labeled peaks and structures}\]

\[\text{Diagram with m/z values and structural representation}\]
Reaction of $5,6\,\alpha\,-\text{epoxy-}5\,\alpha\,-\text{cholestane (CLVIII)}$ with acetonitrile and sodium azide in presence of anhydrous aluminium chloride.

$5,6\,\alpha\,-\text{Epoxy-}5\,\alpha\,-\text{cholestane (CLVIII)}$ was taken in dry acetonitrile and were added anhydrous aluminium chloride and sodium azide. The mixture was stirred for 6 hrs at room temperature. After completion of reaction, the solvent was evaporated and the residue was extracted with chloroform. The organic layer was washed with water, aqueous solution of sodium bicarbonate (5%) and again with water, and dried. Removal of chloroform left an oil which was chromatographed on a silica gel column and a compound with m.p. $181^\circ C$ was obtained.

\[
\text{(CLVIII)}
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\[
\text{(CLXI)}
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Characterization of the compound melting at $181^\circ C$ as 5-hydroxy-5\,\alpha\,-cholest-6\beta (1')-5\,'\text{-methyltetazole (CLXI)}$.

The elemental analysis of the compound, m.p.$181^\circ C$ corresponded to the molecular formula $C_{29}\,H_{50}\,N_4\,O$. The IR spectrum of the compound exhibited bands at 3300 (OH), 1510, 1460 and 1375 cm\(^{-1}\) (C=\text{N}, \text{N=N})\text{.16,17. These values suggested}

the presence of tetrazole moiety. The $^1$H-NMR spectrum of the compound displayed a multiplet for one proton centered at 6 4.21 which was assigned to C6- $<$ H (W1/2 = 5Hz, equatorial). A sharp singlet integrating for three protons appeared at 6 2.57 due to the methyl protons of the tetrazole moiety. The hydroxyl proton (exchangeable with deuterium) appeared at 6 2.11 as a broad singlet. Other methyl protons were observed at 6 1.05 (Cl0-CH$_3$), 0.67 (Cl3-CH$_3$), 0.95 and 0.84 (other side chain methyl protons). The mass spectrum of the compound showed the molecular ion peak at m/z 470 (M$^+$). Some other characteristic fragment ion peaks were recorded at m/z 455, 453, 452, 387, 386, 368, 357 and 438. The fragmentation pattern of these ions were given in scheme. On the basis of above evidences, the compound having m.p. 181°C was characterized as 5-hydroxy-5$<$-cholest-6$/$ (l')-5'$-$methyltetrazole (CLXI).

**Scheme**
Reaction of $3\beta$-chloro-5,6-epoxy-5-cholestane (CLIX) with acetonitrile and sodium azide in the presence of anhydrous aluminium chloride.

To a solution of $3\beta$-chloro-5,6-epoxy-5-cholestane (CLIX) in acetonitrile were added anhydrous aluminium chloride and sodium azide. After usual work up of the reaction mixture and chromatography over silica gel, a compound having m.p. 174°C was isolated.

Characterization of the compound with m.p. 174°C as $3\beta$-chloro-5-hydroxy-5-cholest-6(1')-5'-methyltetrazole (CLXII).

The compound having m.p. 174°C showed the molecular composition C$_{29}$ H$_{49}$ N$_{4}$ OCl (positive Beilstein test). The IR spectrum of the compound exhibited bands at 3400 (OH), 1515, 1475, 1380 (C=N, N=N)$^{16,17}$ and 760 cm$^{-1}$ (C-Cl). The $^1$H-NMR spectrum of the compound displayed two multiplets for one proton each at $\delta$ 4.46 and 4.22 and were assigned to C3-$\alpha$ H ($W_1/2=16$Hz, axial)$^{39}$ and C6-$\alpha$ H ($W_1/2=4.5$Hz, equatorial)$^{39}$ respectively. Signal for the methyl protons of tetrazole moiety appeared at $\delta$ 2.62 as a sharp singlet. The hydroxyl
proton (exchangeable with deuterium) appeared at 62.28 as a broad singlet. Other methyl protons were observed at 6 1.08 (C10-CH₃), 0.76 (C13-CH₃), 0.95 and 0.84 (other side chain methyl protons). On the basis of above values, the compound melting at 174°C was characterized as 3β - chloro-5-hydroxy-5α-cholest-6β (1')-5'-methyldizazole (CLXII). This structure was further supported by mass spectral studies. The mass spectrum showed the molecular ion peak at m/z 504/506 (M⁺) and other important fragment ions peaks at m/z 489/491, 486/488, 468, 450, 421/423, 420/422, 403/405, 402/404, 391/393, 388/390 and 366 as shown in scheme.

Scheme
Reaction of 3β- -acetoxy-5,6 < -epoxy-5< -cholestane (CLX) with acetonitrile and sodium azide in presence of anhydrous aluminium chloride.

To a stirred solution of 3β -acetoxy-5,6< -epoxy-5< -cholestane (CLX) in acetonitrile was added sodium azide and anhydrous aluminium chloride. After usual work up and column chromatography a compound having m.p. 221°C was isolated.

Characterization of the compound having m.p. 221°C as 3β- -acetoxy-5-hydroxy-5< -cholesterol-6β (1')-5'-methyl tetrazole (CLXIII).

The elemental analysis for the compound having m.p. 221°C corresponded to the molecular composition C31 H52 N4O3. Its IR spectrum exhibited bands at 3375 (OH), 1720 (CH₃COO), 1520, 1465, 1375 (C=N, N=N) 1250 and 1030 cm⁻¹ (C=O). The ¹H-NMR spectrum of the compound showed two multiplets for one proton each at 6 5.1, 4.23 and were assigned to C3-<H (W 1/2=16 Hz, axial)³⁹ and C6-<H (W 1/2=4Hz, equatorial)³⁹ respectively. A sharp singlet exhibited at 6 2.57 integrating for three protons was due to the methylprotons of the
tetrazole moiety. The hydroxyl proton (exchangeable with deuterium) appeared at δ 2.24 as a broad singlet. The methyl protons of the acetoxy group appeared at δ 2.01 as a sharp singlet. Other methyl protons were observed at δ 1.21 (Cl0-CH₃), 0.72 (Cl3-CH₃), 0.91 and 0.83 (other side chain methyl protons). The mass spectrum of the compound gave molecular ion peak at m/z 528 (M⁺) followed by other important fragment ion peaks at m/z 513, 510, 469, 468, 450, 445, 444, 426, 415 and 366 as shown in scheme. On the basis of all these data, the compound having m.p. 221°C was characterized as 3β-acetoxy-5-hydroxy-5α-cholest-6/3 (1')-5'-methyltetrazole (CLXIII).

Scheme
EXPERIMENTAL
Reaction of cholest-5-ene (CXLIX) with bromine, acetonitrile and sodium azide: 5-Bromo-6β-acetamido-5α-cholestane (CLV) and 5-bromo-5α-cholest-6β (1')-5'-methyltetrazole (CLII).

Cholest-5-ene (2g; 5.4 m mol) was taken in acetonitrile (40 ml) and to this was added anhydrous aluminium chloride (2g, 15.0 m mol). The suspension was cooled in ice-salt bath, while being stirred magnetically when the content has cooled down to 0°C, bromine (0.8g; 50m mol) then sodium azide (1.5g; 23.2 m mol) were added successively. The stirring was continued for 2 hrs at 0°C and again 2 hrs at room temperature. The progress of reaction was monitored by TLC. The solvent was removed under reduced pressure and residue was extracted with chloroform. Chloroform layer was washed with water, sodium bicarbonate (5%) again with water and dried (anhyd. Na₂SO₄). Chloroform was evaporated under reduced pressure and the residue was chromatographed over silica gel. Elution with light petroleum ether/ether (5:1) provided a solid compound which was recrystallized from acetone to yield 5-bromo-6β-acetamido-5α-cholestane (CLV) (0.45g; 0.88 m mol), m.p. 172°C.

Analysis found : C, 68.4; H, 9.9; N, 2.6
C₂₉H₅₀NOBr required : C, 68.50; H, 9.84; N, 2.75%

IR : ν max 3420 (NH), 1670 (-CO-NH-) and 730 cm⁻¹ (C-Br).

¹H-NMR : δ 5.8 (br, 1H, NH), 3.2 (m, 1H, W 1/2=4.5 Hz, C6-CH₃), 2.1 (s, 3H, -CO-CH₃), 1.2 (C10-CH₃), 0.72 (C13-CH₃), 0.97 and 0.84 (other methyl protons).
Further elution with light petroleum ether/ether (3:1) furnished a solid which was recrystallized from acetone to
afford 5-bromo-5-c-cholest-6β-(1')-5'-methyltetrazole (CLII) (1.1g, 2.06 m mol), m.p. 156°C.

Analysis found : C, 65.39; H, 9.2; N, 10.4
C₂₉H₄Br requires : C, 65.290; H, 9.19; N, 10.54%
IR : ν max 1530, 1460, 1380 (C=N, N=N) 16',17 and 740 cm⁻¹ (C-Br).

¹H-NMR : 6 3.1 (m, 1H, W 1/2 = 5Hz, C6-<H)³⁹, 2.5 (s, 3H, -N-CN-CH₃), 1.02 (Cl0-CH₃), 0.7 (Cl3-CH₃), 0.96 and 0.81 (other methyl protons).

MS : M⁺ 532/534 (5.20/5.18; C₂₉H₄₉H₄Br), 517/519 (5.00/4.99), 453 (10.00), 452 (12.75; C₂₉H₄₈N₄), 449/451 (6.40/6.38), 448/450 (9.50/9.47; C₂₇H₄₅Br), 438 (11.20), 419/421 (5.40/5.37), 392/394 (8.30/8.28), 391/393 (9.75/9.73), 378/380 (8.70/8.69), 377/379 (13.10/13.08), 368 (14.25; C₂₇H₄₄), 312 (12.80), 311 (14.00), 308/310 (9.75/9.74), 307/309 (11.90/11.88), 305 (9.00), 298 (10.00), 297 (13.30), 294/296 (11.20/11.18), 293/295 (15.30/15.29), 270 (3.80), 269 (5.40), 268 (7.45), 267 (5.00), 252 (5.50), 251 (10.25), 250 (6.10), 248 (4.80), 246 (4.60), 245 (4.60), 217 (4.10), 216 (10.25), 215 (4.10), 189 (5.10), 188 (7.50), 187 (3.80), 178 (3.50), 177 (5.75), 175 (6.20), 174 (5.00), 173 (3.10), 162 (3.25), 161 (5.75), 160 (7.20), 159 (4.20), 158 (10.40), 147 (9.80), 146 (5.50), 145 (9.80), 135 (10.00), 134 (6.10), 133 (7.50), 130 (14.10), 129 (8.50), 121 (17.75), 120 (10.00), 119 (6.20), 118 (14.70), 106 (24.25), 105
(12.50) 104 (19.30), 103 (7.20), 95 (42.10), 94 (23.75), 93
(38.50), 92 (10.00), 91 (25.50), 84 (8.40), 83 (12.10), 82
(19.00), 81 (31.00), 80 (19.80), 79 (34.30), 77 (12.40), 71
(12.40), 70 (7.25), 69 (29.00), 68 (10.25), 67 (32.10), 58
(24.30), 57 (30.10), 56 (15.75), 55 (10.25), 54 (47.20), 45
(30.25), 44 (10.00), 43 (27.25), 42 (100.00), 41 (41.00), 40
(17.25).

Reaction of 3β-chlorocholest-5-ene (CL) with bromine,
acetonitrile and sodium azide: 3β-Chloro-5-bromo-6β-aceta-
mido-5α-cholestane (CLVI) and 3β-chloro-5-bromo-5α-
cholest-6β(1')-5'-methyltetrazole (CLIII).

To a suspension of 3β-chlorocholest-5-ene (2g, 4.9 m
mol) in acetonitrile (40 ml) was added anhydrous aluminium
chloride (2g, 15.0 m mol). The suspension was cooled in ice-
salt bath with continuous stirring. To this mixture, bromine
(0.8g; 5.0 m mol) and sodium azide (1.5g; 23.1 m mol) were
added successively and the stirring continued at 0°C and
room temperature for 2 hrs each. After the completion of
reaction, it was worked up as described earlier andchromat-
ographed over silica gel. Elution with light petroleum ether/
ether (10:1) provided 3β-chloro-5-bromo-6β-acetamido-5α-
cholestane (CLVI), (0.5g; 0.92 m mol) as an oil.

Analysis found: C, 64.1; H, 9.1; N, 2.5

C29H49NOBrCl requires: C, 64.14, H, 9.09, N, 2.58%
IR : $\nu$ max 3410 (NH), 1860 (NH-CO-CH₃) and 715 cm$^{-1}$ (C-Cl and C-Br).

$^1$H-NMR : 6.41 (mc, 1H, $W_1/2 = 16$ Hz, C3- $\leftrightarrow$ H)40, 3.76 (mc, 1H, $W_1/2 = 4.5$ Hz, C6- $\leftrightarrow$ H), 2.01 (s, 3H, -CO-CH₃), 1.26 (C10-CH₃), 0.68 (C13-CH₃), 0.95 and 0.82 (other methyl protons).

MS : $M^+$ 541/543/545 (3.80/4.92/1.20; C₂₉ H₄₉ NOBrCl), 526/528/530 (4.90/6.35/1.54), 505/507 (7.10/7.09) 483/485/487 (6.00/7.77/1.90), 462/464 (6.20/2.00), 461/463 (8.50/2.81), 447/449 (7.40/7.37), 446/448 (9.50/9.48), 429/431 (8.30/2.74), 428/430/432 (4.00/5.18/1.23), 426 (6.10), 425 (20.25; C₂₉ H₄₇ NO), 393 (14.40), 366 (24.30), 351 (16.00), 319 (4.50), 318 (5.10), 317 (4.50), 308 (4.50), 307 (5.00), 306 (6.10), 305 (4.50), 304 (17.70), 303 (6.00), 256 (3.80), 255 (3.80), 254 (5.20), 250 (11.30), 249 (6.30), 228 (5.00), 226 (12.20), 225 (14.10), 212 (13.75), 211 (15.00), 198 (5.00), 197 (5.00), 176 (3.40), 175 (5.10), 1745 (6.60), 173 (5.30), 172 (4.10), 160 (7.50), 159 (6.10), 158 (5.00), 156 (6.20), 149 (9.00), 148 (7.10), 147 (5.25), 146 (10.25), 145 (4.80), 134 (8.70), 133 (6.00), 132 (10.00), 131 (5.00), 130 (6.30), 120 (11.20), 119 (8.00), 118 (11.30), 106 (10.00), 105 (7.50), 104 (17.50), 103 (15.10), 102 (15.00), 94 (30.00), 93 (11.20), 92 (27.50), 91 (20.00), 90 (15.75), 84 (14.75), 82 (29.25), 81 (27.25), 80 (29.30), 79 (27.50), 78 (20.00), 77 (10.50), 76 (7.50), 70 (12.50), 69 (6.30), 68 (22.50), 67 (8.70), 66 (20.00), 56 (32.20), 55 (10.00), 54
Further elution with light petroleum ether/ether (5:1) afforded 3β-chloro-5-bromo-5α-cholest-6β (1')-5'-methyl-tetrazole (CLIII), (1.0g; 1.76 m mol) as an oil.

Analysis found: C, 61.3; H, 8.5; N, 9.8

C_{29} H_{48} N_{4} Br Cl requires: C, 61.31, H, 8.52, N, 9.86%

IR: ν max 1525, 1460, 1375 (C=N, N=N) 1617, 740 and 720 cm⁻¹ (C-Cl and C-Br).

^1H-NMR: δ 3.95 (mc, 1H, W 1/2 = 16 Hz, C3-<H) 39, 3.6 (mc, 1H, W 1/2 = 4 Hz, C6-<H) 40, 2.52 (s, 3H, -N-CN-CH₃), 1.2 (C10-CH₃), 0.7 (C13-CH₃), 0.91 and 0.80 (other methyl protons).

MS: M⁺ 566/568/570 (3.50/4.51/1.08; C_{29} H_{48} N_{4} BrCl), 551/553/555 (4.90/6.35/1.54), 531/533 (6.50/6.45), 530/532 (7.20/7.18), 483/485/487 (5.20/6.74/1.61), 482/484/486 (6.75/8.75/2.13), 472/474 (8.00/2.64), 453/455/457 (3.75/4.85/1.17), 452 (9.25), 451 (3.75), 450 (13.00), 446/ 448 (8.80/8.78), 402/404 (10.25/3.39), 366 (17.20), 350 (12.75), 344 (7.50), 334 (5.10), 318 (5.10), 317 (5.25), 3.08 (5.00), 307 (4.50), 306 (4.50), 305 (9.20), 304 (6.20), 303 (10.50), 257 (4.80), 256 (7.30), 255 (4.80), 254 (5.20), 250 (14.25), 249 (5.40), 226 (8.40), 225 (9.75), 212 (10.00), 211 (11.25), 188 (5.00), 187 (5.00), 186 (3.25), 160 (17.25), 159 (8.50), 158 (5.00), 156 (10.25), 147 (9.00), 146 (9.10), 134 (10.00), 133 (8.40), 132 (5.25), 131 (5.25), 130 (7.70), 129 (6.10), 120 (10.25),
Reaction of 3β-acetoxycholest-5-ene (CLI) with bromine acetonitrile and sodium azide: 5-Bromo-6β-acetamido-5α-cholest-3-ene (CLVII) and 5-bromo-5α-cholest-3-en-6β (1')-5' methyltetrazole (CLIV).

The 3β-acetoxycholest-5-ene (2g, 4.67 m mol) was dissolved in acetonitrile (40 ml) and to this mixture was added anhydrous aluminium chloride (2g; 15.0 m mol). The suspension was cooled to 0°C in an ice-salt bath while being stirred magnetically. To this suspension, bromine (0.8g; 5.0 m mol) and sodium azide (1.5g; 23.1 m mol) were added successively. The stirring was continued for 2 hrs at 0°C and 2 hrs at room temperature. After the completion of the reaction, the mixture was worked-up as usual and chromatographed over silica gel. Elution with light petroleum ether/ether (5:1) provided a solid compound which was recrystallized from acetone to yield 5-bromo-6β-acetamido-5α-cholest-3-ene (CLVII) (0.3g; 0.592 m mol) m.p. 159°C.
Analysis found: C, 68.7; H, 9.5; N, 2.8

C₂₉H₄₈NOBr requires: C, 68.75; H, 9.55; N, 2.76%

IR: max 3430 (NH), 1670 (–NH–CO–CH₃), 1625 (C=C) and
730 cm⁻¹ (C–Br).

¹H-NMR: δ 6.2 (br, 1H, NH), 5.5–5.4 (mc, 2H, C3 and C4 vinyl
protons), 3.2 (mc, 1H, W ½ = 5Hz, C6–CH3)²⁹, 2.1 (s, 3H,
–CO–CH₃); 1.2 (C10–CH₃), 0.7 (C13–CH₃), 0.97 and 0.83 (other
methyl protons).

MS: M⁺ 505/507 (6.75/6.73; C₂₉H₄₈NOBr), 490/192
(5.00/4.97), 447/449 (8.75/8.74), 446/448 (9.80/9.77), 426
(10.30), 425 (9.60, C₂₉H₄₇NO), 411 (14.25), 392/394
(5.75/5.72), 383 (11.30), 382 (14.25), 368 (12.20), 366
(24.40; C₂₇H₄₂), 332 (4.40), 331 (6.20), 330 (7.50), 329
(5.00), 328 (9.20), 327 (4.10), 302 (4.20), 301 (7.50), 300
(4.20), 276 (10.25), 275 (12.30), 274 (8.20), 273 (4.10), 268
(3.50), 267 (3.50), 263 (2.50), 262 (2.10), 255 (4.50), 254
13.75), 246 (5.75), 245 (10.20), 244 (5.00), 228 (8.10), 227
(9.75), 226 (9.75), 225 (13.10), 214 (9.10), 213 (11.70), 212
(10.00), 211 (14.10), 200 (6.40), 199 (9.60), 198 (7.00), 197
(4.30), 188 (7.20), 187 (6.90), 186 (6.50), 185 (6.90), 184
(4.00), 174 (3.70), 173 (5.75), 172 (5.75), 171 (3.60), 162
(4.90), 161 (4.90), 160 (7.60), 159 (5.00), 158 (8.30), 157
(7.10), 157 (7.10), 146 (10.25), 145 (13.00), 144 (10.25),
143 (6.00), 142 (3.75), 134 (9.30), 132 (12.50), 130 (10.00),
120 (13.30), 119 (11.25), 118 (10.10), 111 (4.80), 106
(15.75), 105 (10.25), 104 (17.00), 103 (6.60), 94 (27.90), 93
Further elution with light petroleum ether/ether (3:1) furnished a solid compound, which was recrystallized from acetone to afford 5-bromo-5'-cholest-3-en-6/3 (1'-5'-methyltetrazole (CLIV) (1.2g; 2.26 m mol) m.p. 178°C. Analysis found: C, 65.5; H, 8.9; N, 10.5

C29 H47 N4 Br requires: C, 65.52; H, 8.91; N, 10.54%

IR: \( \nu \) max 1520, 1465, 1380 (C=N, N=N), 1617, 1620 (C=C) and 730 cm\(^{-1}\) (C-Br).

\( ^{1}H\)-NMR: \( \delta \) 5.53-5.45 (mc, 2H, C3 and C4-vinyl protons), 3.06 (mc, 1H, \( \omega \) 1/2 = 4.5 Hz, C6-\( \omega \)H), 2.56 (s, 3H, -N-CN-CH3), 1.15 (Cl0-CH3), 0.71 (Cl3-CH3), 0.92 and 0.80 (other methyl protons).

MS: \( M^+ \) 530/532 (5.75/5.73; C29 H47 N4 Br), 515/517 (6.00/5.98), 451 (7.20), 450 (8.30; C29 H46 N4), 447/449 (8.50/8.47), 446/448 (10.00/9.98), 436 (14.25), 417/419 (5.50/5.48), 368 (17.70), 367 (8.10), 366 (27.20; C27 H42), 330 (7.50), 329 (5.00), 328 (3.75), 301 (3.30), 300 (6.40), 299 (3.30), 298 (3.70), 276 (4.00), 275 (8.20), 274 (6.10), 273 (5.00), 268 (5.00), 267 (5.00), 266 (9.60), 265 (4.75),
5,6-Epoxy-5-cholestane (CLVIII)

Cholest-5-ene (6g) in chloroform (40 ml) was treated with a solution of perbenzoic acid (1.1 mol equivalent) in chloroform and left at -8°C for 20 hrs. The reaction was washed successively with ice-cold aqueous sodium bicarbonate solution (5%), water, aqueous sodium thiosulphate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent yielded (CLVIII) as an
oil which was crystallized from acetone as needles (4.5g), m.p. 76°C (reported\(^4^0\), m.p. 76°C).

**Reaction of 5,6-epoxy-5-cholestane (CLVIII) with acetonitrile and sodium azide:** 5-Hydroxy-5-cholest-6\(\beta\) (1')-5'-methyltetrazole (CLXI).

To a stirred solution of 5,6-epoxy-5-cholestane (CLVIII) (2.0g; 5.18 m mol) in acetonitrile (20 ml) were added anhydrous aluminium chloride (catalytic amount) and sodium azide (equimolar). Stirring was continued for 6 hrs at room temperature. After completion of the reaction, the solvent was evaporated at reduced pressure and the residue was extracted with chloroform. The organic layer was washed with water, 5% aqueous solution of sodium bicarbonate and again with water, and dried. Removal of chloroform left an oil which was chromatographed on a silica gel (40 g) column.

Elution with light petroleum ether/ether (5:1) provided a solid compound which was recrystallized from acetone to yield, 5-hydroxy-5-cholest-6\(\beta\) (1')-5'-methyltetrazole (CLXI), (1.6g; 3.4 m mol), m.p. 181°C.

Analysis found : C, 74.1; H, 10.7; N, 11.0

C\(_{29}\)H\(_{50}\)N\(_4\)O requires : C, 73.99, H, 10.71; N, 11.9%

IR : \(\nu\) max 3300 (OH), 1510, 1460 and 1375 cm\(^{-1}\) (C=N, N=N)\(^{16,17}\).

\(^1\)H-NMR : \(\delta\) 4.21 (mc, 1H, W 1/2 = 5Hz, C6-\(\alpha\)H)\(^{39}\), 2.57 (s, 3H,
-N-CN-CH₃), 2.11 (br, 1H, OH), 1.05 (C₁₀-CH₃), 0.67 (C₁₃-CH₃), 0.95 and 0.84 (other methyl protons).

**MS**

M⁺ 470 (7.00; C₂₉H₅₀N₄O), 455 (8.10), 453 (8.50), 452 (9.30), 438 (7.70), 387 (12.25), 386 (14.30; C₂₇H₄₆O), 368 (13.10; C₂₇H₄₄), 357 (7.50), 330 (7.20), 329 (9.50), 316 (8.50), 315 (10.00), 283 (3.90), 282 (3.50), 281 (5.20), 267 (4.40), 266 (4.40), 265 (10.25), 264 (5.30), 263 (8.75), 249 (6.40), 248 (4.40), 247 (10.75), 246 (5.00), 228 (8.70), 227 (9.90), 214 (8.90), 213 (10.30), 212 (2.40), 211 (8.75), 194 (8.00), 193 (4.30), 192 (14.20), 136 (6.40), 135 (3.20), 134 (17.50), 133 (10.00), 132 (9.90), 131 (4.00), 130 (10.50), 129 (8.10), 120 (12.00), 119 (5.00), 118 (14.30), 117 (20.70), 116 (9.20), 115 (4.80), 108 (16.75), 107 (6.40), 106 (20.00), 105 (5.10), 104 (21.50), 103 (11.25), 94 (33.30), 93 (7.50), 92 (28.60), 91 (4.90), 90 (26.75), 89 (4.50), 84 (10.00), 83 (20.00), 82 (19.10), 81 (9.60), 80 (40.50), 79 (12.20), 70 (21.50), 69 (12.00), 68 (34.60), 67 (35.30), 66 (23.80), 65 (8.90), 57 (52.40), 56 (11.50), 55 (54.80), 54 (17.30), 53 (10.50), 45 (41.20), 44 (35.30), 43 (100.00), 42 (15.30), 41 (42.10), 40 (19.00).

3β-Cloro-5,6-epoxy-5-cholestan-3β (CLIX)

3β-Chlorocholest-5-ene (11g) in chloroform (100 ml) was treated with a solution of perbenzoic acid (1.1 molequivalent) and left for 20 hrs at -8°C. The reaction mixture was then washed successively with ice-cold sodium bicarbonate solution (5%), water, sodium thiosulphate
solution (50%) and again with water and dried. Evaporation of the solvent yielded (CLIX) as oil which was crystallized from acetone as needle (8.1g), m.p. 89°C (reported m.p. 89.5-90.5°C).

Reaction of 3β-chloro-5,6-epoxy-5-cholestane (CLIX) with acetonitrile and sodium azide: 3β-Chloro-5-hydroxy-5-cholest-6β(1')-5'-methyltetrazole (CLXII).

To a stirred solution of 3β-chloro-5,6-epoxy-5-cholestane (CLIX) (2.0g, 4.74 m mol) in acetonitrile (20 ml) was added anhydrous aluminium chloride (catalytic amount) and sodium azide (equimolar). Stirring was continued for 6 hrs. at room temperature. After completion of the reaction, the reaction mixture was worked up as usual and chromatographed over silica gel column. Elution with light petroleum ether/ether (5:1) provided a compound which was crystallized from acetone to yield 3β-chloro-5-hydroxy-5-cholest-6β (1')-5'-methyltetrazole (CLXII), (1.75g, 3.46 m mol), m.p. 174°C.

Analysis found: C, 70.1; H, 9.6; N, 11.0

C29 H49 N4 OCl requires: C, 68.94; H, 9.77; N, 11.09%

IR: ν max 3400 (OH), 1515, 1475, 1380 (C=N, N=N)16,17, and 760 (C-Cl).

1H-NMR: δ 4.46 (mc, 1H, W 1/2 = 16 Hz, C3-<H)40, 4.22 (mc, 1H, W 1/2 = 4.5 Hz, C6-<H)39, 2.62 (s, 3H,-N-CN-CH3) 2.28 (br, 1H, OH), 1.08 (Cl0-CH3), 0.76 (Cl3-CH3), 0.95 and 0.84 (other methyl protons).
**Reaction of 3β-acetoxy-5,6-epoxy-5-cholestane (CLX) with acetonitrile and sodium azide: 3β-Acetoxy-5-hydroxy-5-cholest-6 β (1')-5'-methyltetrazole (CLXIII).**

To a stirred solution of 3β-acetoxy-5,6-epoxy-5-cholestane (CLX) (2.0g; 4.51 m mol) in acetonitrile (20 ml)
was added anhydrous aluminium chloride (catalytic amount) and sodium azide (equimolar). Stirring was continued for 6 hrs. at room temperature. After completion of reaction, the reaction mixture was worked up as usual and chromatographed over silica gel column. Elution with light petroleum ether/ether (5:1) provided a solid compound which was recrystallized from acetone to afford, 3\beta-acetoxy-5-hydroxy-5α-cholest-6β(1')-5'-methyltetrazole (CLXIII), (1.70 g; 3.22 m mol), m.p. 221°C.

Analysis found : C, 70.3; H, 9.9 ; N, 10.7

C\textsubscript{31} H\textsubscript{52} N\textsubscript{4} O\textsubscript{3} requires : C, 70.41; H, 9.91; N 10.59%

IR : \text{\textgamma} max 3375 (OH), 1720 (CH\textsubscript{3} COO), 1520, 1465, 1375 (C=N, N=N)\textsuperscript{16,17}, 1250 and 1030 cm\textsuperscript{-1} (C-O).

\textsuperscript{1}H-NMR : \delta 5.1 (mc, 1H, W 1/2 = 16 Hz, C3-\textless H)\textsuperscript{40}, 4.23 (mc, 1H, W 1/2 = 4 Hz, C6-\textless H)\textsuperscript{39}, 2.57 (s, 3H, -N-CN-CH\textsubscript{3}), 2.24 (br, 1H, OH), 2.01 (s, 3H, OCOCH\textsubscript{3}), 1.21 (Cl0-CH\textsubscript{3}), 0.72 (Cl3-CH\textsubscript{3}), 0.91 and 0.83 (other methyl protons).

MS : M\textsuperscript{+} 528 (7.60; C\textsubscript{31} H\textsubscript{52} N\textsubscript{4} O\textsubscript{3}), 513 (7.00), 510 (8.25), 469 (10.50), 468 (12.10; C\textsubscript{29} H\textsubscript{48} O), 450 (15.30; C\textsubscript{29} H\textsubscript{46}), 445 (8.40), 444 (9.75), 426 (10.75; C\textsubscript{29} H 46 O\textsubscript{2}), 415 (7.80), 410 (16.20), 366 (23.00; C\textsubscript{27} H\textsubscript{42}), 339 (6.20), 338 (9.60), 337 (5.75), 254 (4.80), 253 (6.10), 252 (5.00), 246 (5.20), 245 (5.25), 228 (7.40), 227 (9.75), 226 (8.25), 225 (12.00), 214 (8.50), 213 (9.90), 212 (9.50), 211 (14.50), 210 (4.20), 206 (2.75), 205 (5.75), 204 (10.20), 203 (6.00), 201 (4.30), 200 (7.40), 199 (4.50), 198 (4.50), 197 (3.75), 162
(5.00), 161 (5.20), 160 (5.50), 159 (4.10), 158 (6.40), 157 (4.10), 156 (7.20), 155 (3.75), 148 (6.50), 147 (5.10), 146 (6.00), 145 (5.10), 144 (12.00), 143 (10.00), 142 (7.10), 135 (9.60), 134 (13.25), 133 (7.50), 122 (14.50), 121 (9.75), 120 (14.75), 119 (14.75), 118 (20.25), 117 (40.00), 116 (10.50), 106 (24.30), 105 (60.10), 104 (37.30), 103 (15.25), 95 (11.90), 94 (20.25), 93 (29.00), 92 (35.30), 91 (10.75), 90 (40.30), 89 (12.25), 84 (15.25), 83 (25.75), 80 (13.70), 79 (12.25), 78 (32.10), 77 (30.00), 76 (19.25), 75 (9.60), 61 (17.25), 60 (14.00), 59 (11.20), 44 (10.50), 43 (100.00), 42 (19.30), 41 (41.20), 40 (38.70).


