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# THIOSTEROIDS—XXVII[1]

## STEROIDAL TRANSANNULAR 2α,5α-EPISULPHIDE—I. SYNTHESES OF 5α-CHOLESTAN-2α,5-EPISULPHIDE DERIVATIVES

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**Abstract**—The attempted dehydration of 5-acetylthio-5α-cholestan-3β-ol (**3**) to 5α-cholest-2-ene-5-thiol (**1a**) gave rise to acetyl migration, leading to 3α-acetoxy-5α-thiol (**8**), established by isolation of the supposed intermediate, 3α-O-5α-S-thiol acetonium ion as the perchlorate (**6**). The reaction of **1a**, successfully derived from the 2-ene-5β,6β-epoxide (**11**), with halogen and with $Pb(OAc)_4$ furnished 3β-halo-2α,5α-episulphide (**13a**), **13b** and 3β-acetoxy-2α,5α-episulphide (**14a**), respectively. The bromide (**13a**) on treatment with AcOK afforded the 3β-OH derivatives (**14a**, **14b** and **14c**). Reductions with $NaBH_4$, $LiAlH_4$, and $LiAlH(O_tBu)_3$ of the 3-oxo compound (**15**) derived from **14c** yielded a mixture of the epimeric alcohols (**14c** and **16a**), which were studied by means of VPC and TLC. These mechanisms are discussed in terms of the sulphur participation at the electron deficient $C_3$. $Pb(OAc)_4$ oxidation of the 4-ene-2β-thiol (**22b**), a homoallyl thiol, failed to give the expected 2β,5β-epithio derivative.

RECENTLY, a number of steroidal transannular 2α,5α- and 2β,5β-epoxides, i.e. comprising the 7-oxabicyclo[2.2.1]-heptane system, have been synthesized starting with compounds having 2-en-5α- and 2-en-5β-ol in their structures respectively.[1,2] In 1957, Martin and Bartlett[3] concluded from their studies on kinetics of the solvolysis of *exo*- and *endo*-2-chloro-7-oxabicyclo[2.2.1]heptane that the bridging oxygen did not exert extraordinary participation in the transition state resulting from the *endo* isomer. In this respect, a comparison of sulphur with oxygen in the bridge would be interesting because a S atom often displays unique properties. We wish to describe now the synthesis of 5α-cholestan-2α,5-episulphide with and without a substituent at $C_3$, and their unique properties.

The 7-thiabicyclo[2.2.1]heptane system was little known, and had been prepared only by Diels–Alder reaction with benzo-C-thiophene,[4] until Corey and Block[5] recently synthesized 2,5-bis *endo* dichloro-7-thiabicyclo[2.2.1]-heptane by the intramolecular addition of sulphur dichloride with 1,4-cyclohexadiene. As a key intermediate for our syntheses, we chose 5α-cholest-2-ene-5-thiol (**1a**), whose structure is analogous to the 2-en-5α-ol. The preparation of **1a** was undertaken by two independent sequences. Firstly, it was attempted starting with 5-acetylthio-5α-cholestan-3β-ol (**3**), readily obtained in quantitative yield by partial hydrolysis of the 3,5-diacetate (**2**)[6] with 1% methanolic hydrogen chloride.* Unfortunately, this attempt was unsuccessful, resulting in rearrangement of the acetyl moiety in compound **3** as follows.

* The partial hydrolysis of **2** with potassium hydrogen carbonate in aqueous methanol gave the 3-monoacetate (**4**) accompanied by a small amount of 3β-hydroxy-5α-thiol. Ref 6.

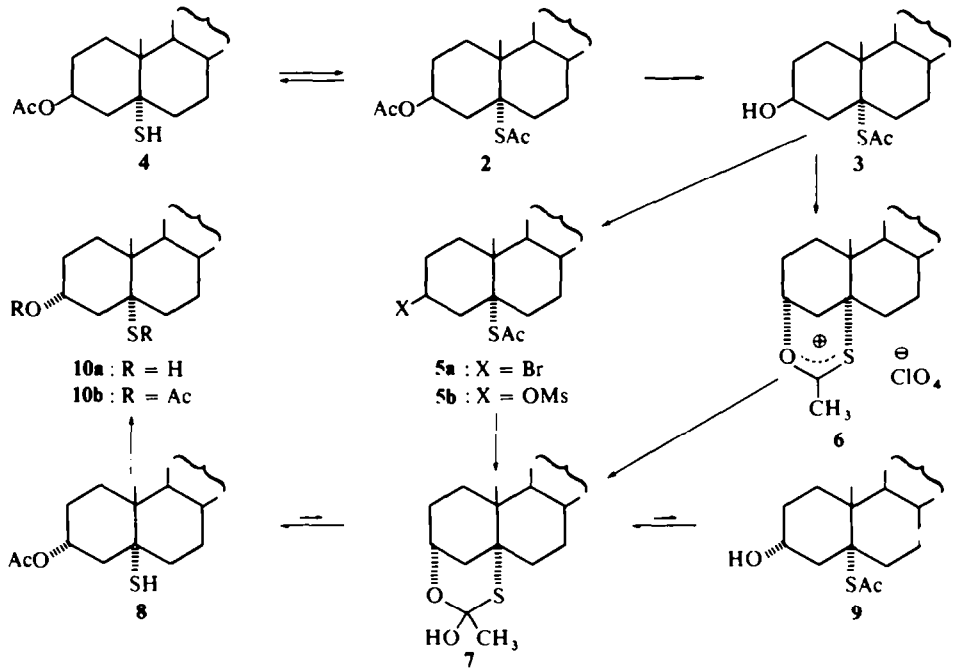



CHART 1

Bromination of the 5-monoacetate (3) with phosphorus tribromide gave in high yield an acetylthio bromide (**5a**), whose NMR spectrum shows a broad multiplet ($W_{h/2}$ = *ca* 25 Hz) at 5·33 τ attributable to the axial proton at $C_3$. The compound **5a**, therefore, was characterized as 3β-bromo-5α-cholestane-5-thiol acetate. Brief treatment of this bromide (**5a**) with collidine resulted in the formation of an acetoxythiol (**8**), which was different from **4**. This compound was also obtained by the same treatment of 3β-mesyloxy-5α-thiol acetate (**5b**), derived from **3** on mesylation. The NMR spectrum of the newly formed compound shows a narrow multiplet ($W_{h/2}$ = 9 Hz) assigned to the equatorial proton at $C_3$. Hence, this compound (**8**) was assumed to be 3α-acetoxy-5α-cholestane-5-thiol. This assignment is also consistent with mechanistic considerations including acetyl migration from the 5α-acetylthio moiety to the developing carbonium ion at $C_3$. Plattner *et al.* have reported analogous acetyl migration accompanied by olefin formation in the conversion of 5-acetoxy-5α-cholestan-3β-ol tosylate to cholest-5-en-3α-ol acetate.[7] The assumption described above was proved by isolation of the supposed thiol acetonium cation as its crystalline perchlorate. Kirk *et al.* achieved the preparation of 6β-substituted 5α-cholestan-3α,5-acetonium perchlorate from the corresponding 3β,5α-diol 5-monoacetate.[8] Thus, when 5-acetylthio-5α-cholestan-3β-ol (**3**) was treated, in the same manner as described by them, successively with acetic anhydride, sulphuric acid and then perchloric acid in methylene chloride, the 3α-O, 5α-S thiol acetonium perchlorate (**6**) was obtained in high yield as considerably stable crystals. The structure of this compound was confirmed by the following spectral data. The IR spectrum exhibits an intense absorption band characteristic of the perchlorate ion at 1100 $cm^{-1}$, and no CO band. The NMR spectrum shows a very sharp singlet ($W_{h/2}$ = 1·5 Hz, cf. TMS $W_{h/2}$ = 1·0 Hz) assigned

to the thiolacetonium methyl protons at 7·03 τ.* This perchlorate on treatment with acetic acid at room temperature for 10 min afforded a mixture of the 3-monoacetate (**8**) and the 5-monoacetate (**9**) in a ratio of 7:1. The minor component, when separated by preparative TLC, gave again a mixture of **8** and **9**. Thus the 5-monoacetate (**9**) could not be isolated in a pure state, but the IR spectrum of the mixture exhibited clearly an absorption band due to the acetylthio group at 1680 $cm^{-1}$ in addition to a band owing to the acetoxyl group at 1730 $cm^{-1}$, giving evidence for the existence of **9**. Kirk *et al.*[8] reported that the hydrolysis of 6β-substituted 5α-cholestan-3α,5-acetonium perchlorate with sodium hydrogen carbonate in aqueous acetone at 20° for 2 min or with acetic acid at 20° for 10 min furnished the 5-monoacetate as a single product, and that heating the salt in aqueous acetic acid at 100° for 40 min afforded the 3-monoacetate.[8] In contrast to this behavior, hydrolysis of the thiol acetonium perchlorate (**6**) with sodium hydrogen carbonate under the conditions they described, gave the 3-monoacetate (**8**) as a single product. It may be noted that in the present case the transient monothio-orthoester (**7**) formed from **6** degrades with the favourable C—S bond fission leading to the 3-monoacetate (**8**). A similar and preferential C—S bond fission is observed in the conversion of 2-imino-1,3-oxathiolane to ethylene sulphide.[10]

As a second method, the preparation of 5α-cholest-2-ene-5-thiol (**1a**) was accomplished according to the procedure described earlier[6] starting with 5β-cholest-2-en-5,6β-epoxide (**11**).[1] The ring-opening reaction of **11** with thiocyanic acid in ether furnished 5-thiocyanato-5α-cholest-2-en-6β-ol (**12a**), which in turn was subjected to mesylation of the OH group at $C_6$, followed by reduction with LAH, affording **1a** in 58% over-all yield. The compound was characterized by its IR and NMR spectra as well as by those of its acetate (**1b**).

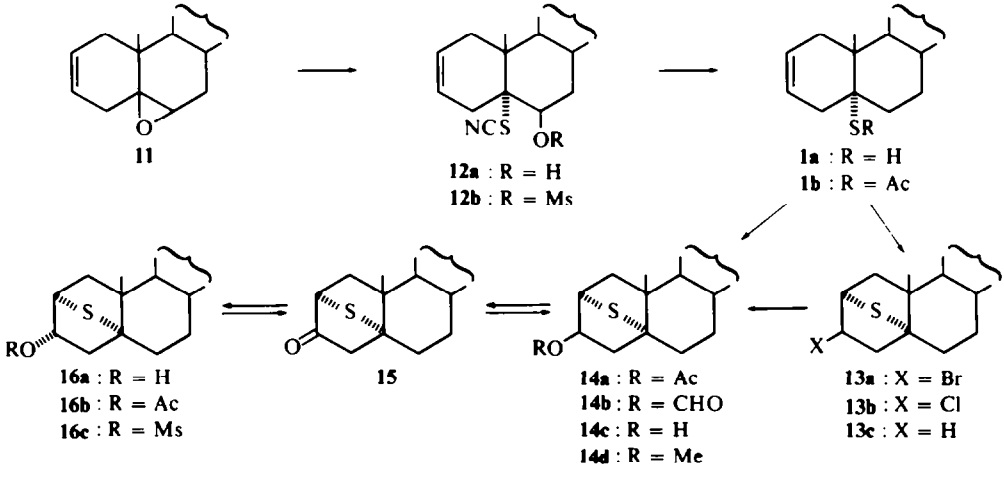



CHART 2

At this stage, the intramolecular reaction of the enethiol (**1a**), a homoallyl thiol system, was explored in two ways. The first approach was performed by bromination of **1a**. Whereas 5α-cholest-2-en-5-ol on treatment with a 1 molar equivalent of bromine

* It was reported that the methyl signal of $\overset{\oplus}{C}H_3\text{--}C{=}O$ appears at 7·07 τ (Ref 9).

in carbon tetrachloride gave 2β,3α-dibromo-5α-cholestan-5-ol, the reaction of **1a** with bromine under the same conditions proceeded rapidly with evolution of hydrogen bromide to give 92% yield of the compound **13a**. This compound, $C_{27}H_{45}SBr$, was characterized as 3β-bromo-5α-cholestan-2α,5-episulphide by its NMR spectrum, which shows a significantly deshielded 10-Me signal at 8·92 τ, a triplet ($J$ = 4·0 Hz: corresponding to a vicinal couplings between the bridge head proton and the two *exo* protons[5]) due to the proton attached to the sulphur bearing carbon at 6·41 τ, and an unresolved multiplet assigned to the proton attached to the bromine bearing carbon at 5·40 τ. Moreover, 100 MHz NMR determination using spin decoupling and/or spin tickling techniques also supports the β-*endo* configuration of the bromine in the compound. The following $J$ values of the proton attached to the bromine bearing carbon were obtained; $J_{2\beta\text{-H}:3\alpha\text{-H}}$ = 4·0, $J_{3\alpha\text{-H}:4\alpha\text{-H}}$ = 9·5, $J_{3\alpha\text{-H}:4\beta\text{-H}}$ = 4·0, and $J_{1\alpha\text{-H}:3\alpha\text{-H}}$ = 2·0 Hz, and these values are in agreement with those reported by Corey and Block.[5] The presence of the 5-membered sulphur heterocyclic ring in compound **13a** was also confirmed by the UV spectrum, in which an absorption maximum was observed at 261 mμ (ε 180) in isooctane solution.[11] Similarly, chlorination of **1a** furnished 3β-*endo*-chloro-5α-cholestan-2α,5-episulphide (**13b**)* in high yield. These reactions may be interpreted by a mechanism involving the initial attack by halogen on either the double bond or the thiol moiety. As observed in the reaction with 5α-cholest-2-en-5-ol, it seems unlikely that the initial attack by halogen, both bromine and chlorine, on the double bond results in the exclusive formation of the single 2β,3β-halonium ion leading to **13a** or **13b**, even though rear attack by halogen would be inhibited owing to the bulkiness of the sulphur atom. Hence. it

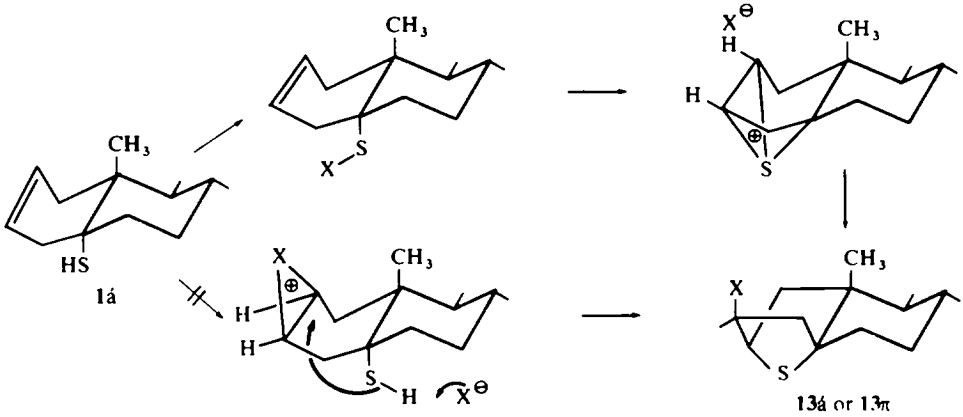



FIG. 1

is more probable that the intramolecular addition of the initially formed sulphenyl halide to the double bond gives rise to the caged sulphonium halide, which in turn forms **13a** or **13b** in keeping with the *trans* relationship between the halogen and the sulphur. Corey and Block also mentioned a similar intermediate in the reaction of sulphur dichloride with 1,4-cyclohexadiene.[5]

LAH reduction of the bromide (**13a**) gave three compounds; 5α-cholest-2-ene-5-thiol (**1a**), a sulphur-containing hydrocarbon (**13c**), and an unidentified material,

* This chloride was formed, though in low yield, on mesylation of 3β-*endo* alcohol (**14c**) (Experimental).

in 10·2, 21·6 and 30·0% yields, respectively. Formation of **1a** may be ascribed to the action of the reagent as a bromine-removing base. The sulphur-containing hydrocarbon (**13c**) was also prepared in improved yield (75%) on reduction of **13a** with sodium borohydride in DMF. Its structure was characterized as 5α-cholestan-2α,5-episulphide based on the NMR spectrum, exhibiting a triplet ($J$ = 3·5 Hz) due to the bridge head proton at 6·37 τ.

The reaction of the bromide (**13a**) with potassium acetate in boiling DMF resulted in substitution at $C_3$. Preparative TLC afforded an acetate (**14a**) in 71·0% yield in addition to a formate (**14b**) in 5·4% yield and an OH derivative (**14c**) in 19·5% yield. That the three compounds have substituents of the same configuration at $C_3$ was elucidated by their interconversion: both the acetate (**14a**) and the formate (**14b**) on reductive hydrolysis with LAH gave the hydroxyl compound (**14c**) and acetylation of **14c** afforded the foregoing acetate (**14a**). Formation of the formate (**17b**) may stem from the reaction of **13a** with the solvent, DMF. Solvolysis of **13a** in methanol furnished the methoxy derivative (**14d**). The 3β-*endo* configurations of all these compounds were deduced from the NMR spectra, showing a triplet ($J$ = 3·0–4·0 Hz) due to the bridge head proton in each case. Furthermore, the chemical shifts of the 10-Me signals in **14a** and **14c** are in good agreement with those predicted from the proximity rule;[12] the spatial proximity of OH in a 1,3-diaxial position to the angular Me group causes a remarkable downward shift of the Me signal and acetylation of the OH group causes a smaller downward shift of the Me signal than the former does. This phenomenon was also observed in 3β- hydroxy- and 3β-acetoxy-5α-cholestan-2α,5-epoxide,[1] as can be seen in Table 1. The retention of configuration in the con-

TABLE 1. CHEMICAL SHIFTS (τ) OF THE 10-METHYL SIGNALS IN THE NMR SPECTRA OF 3-SUBSTITUTED 2α,5α-EPISULPHIDES AND 2α,5α-EPOXIDES

| 3-Substituent | Bridged atom S | | Bridged atom O | |
|---|---|---|---|---|
| | 10-Me | Δτ | 10-Me | Δτ |
| none | 9·05 | -- | 9·04 | -- |
| 3β-*endo*-OH | 8·93 | −0·12 | 8·97 | −0·07 |
| 3β-*endo*-OAc | 8·97 | −0·08 | 9·00 | −0·04 |
| 3α-*exo*-OH | 9·09 | +0·04 | 9·09 | +0·05 |
| 3α-*exo*-OAc | 9·09 | +0·04 | 9·09 | +0·05 |

version of the sulphur bridged bromide (**13a**) to the hydroxyl derivatives, **14a**, **14b** and **14c**, should be attributable to the sulphur participation in the developing carbonium ion at $C_3$, which interferes with the *exo*-attack of the nucleophile. This has been substantiated by the solvolysis rate determinations of the *endo* and *exo* substituted 2α,5α-episulphide together with those of the 2α,5α-epoxide. The results will be presented in the near future.[13]

The second approach to prepare 2α,5α-episulphide was achieved by the reaction of the enethiol (**1a**) with lead tetraacetate. Heusler *et al.*[14] synthesized the transannular 2,19-, 6,19- and 20,18-epoxides from the 2β,6β- and 20-hydroxy compounds, respectively, and proposed the radical mechanism. Of particular interest was that 3β-*endo* acetoxy-5α-cholestane-2α,5-episulphide (**14a**) could be obtained in 86%

yield directly from the reaction of **1a** with lead tetraacetate in boiling cyclohexane under conditions similar to those employed by them. However, 5α-cholest-2-en-5-ol on treatment with lead tetraacetate remained unchanged. Recently, Jones *et al.* reported that oxidation of 5α-cholestan-6β-thiol and 6β-yl disulphide with lead tetraacetate in methanolic chloroform gave 5α-cholestan-6β-yl disulphide, 5α- and 5β-cholestan-6-one, and methyl 5α-cholestan-6β-yl sulphinate.[15] Although oxidation of a sulphur compound with lead tetraacetate has been little known,[16] the high stereospecificity in our oxidation may be comparable with that reported by Readio and Skell.[17] They described the stereoselective *trans* addition of methyl mercaptan to 1-chloro-4-t-butylcyclohexene yielding 2-*trans*-methylthio-1-*trans*-chloro-4-t-butylcyclohexane and proposed a mechanism involving intermediacy of a bridged sulphur radical.[17] In the present case, it is probable that the reaction is initiated by the intramolecular attack on the double bond by 5α-cholest-2-en-5-yl-thiyl radical formed by homolytic cleavage of the S-Pb bond in 5α-cholest-2-en-5-yl thio lead triacetate, yielding the caged 3-membered thiyl radical as shown in Fig. 2.

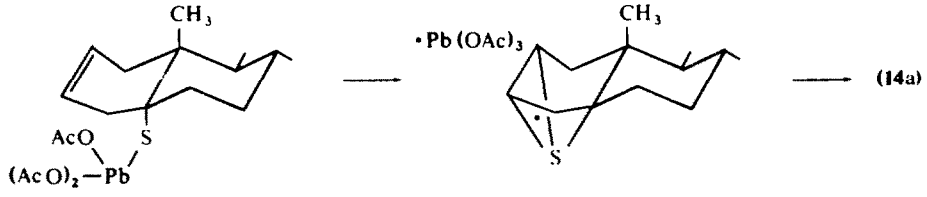



FIG 2.

The oxidation of 3β-hydroxy-5α-cholestan-2α,5-episulfide (**14c**) should be carried out with a mild oxidant, since the S atom is very sensitive to oxidation. Thus, the Oppenauer oxidation of **14c** furnished in 81% yield 3-oxo-5α-cholestan-2α,5-episulphide (**15**), whose structure was characterized by the presence of a 5-membered ring ketone ($\nu_{C=O}$ 1753 $cm^{-1}$) in the IR spectrum. Further confirmation of the structure was given by the NMR spectrum, showing one proton signal assigned to the bridge head proton as a doublet ($J$ = 5·0 Hz) at 6·40 τ. Metal hydride reduction of this ketone afforded a mixture of epimeric alcohols, **14c** and **16a**, which were separated by TLC using an infinite developing method. Alcohol (**16a**) was characterized as 3α-hydroxy-5α-cholestan-2α,5-episulphide based on the following spectral data. The NMR spectrum exhibits one proton signal assigned to the bridge head proton as a doublet ($J$ = 5·0 Hz) at 6·55 τ. In addition, the IR spectrum, using a 20 mm cell, in a dilute carbon tetrachloride solution shows an absorption band owing to an intramolecularly H-bonded OH group at 3551 $cm^{-1}$ ($\Delta\nu$ = 62 $cm^{-1}$). As can be seen in Table 1, it is interesting to note that the chemical shifts of the 10-Me signals in the compound (**16a**) and its acetate (**16b**) have the same value of those in the oxa analogues, and are slightly larger than those in the 3-unsubstituted compounds, though the reason of this shielding is not obvious. In order to determine the ratio of the reduction product, the mixture of the epimeric alcohols was trimethyl-sililated and analyzed by VPC. On the other hand the trimethyl-sililation was replaced by the usual acetylation and the products separated into components, **14a** and **16b**, by preparative TLC. These results are summarized in Table 2. Whereas LAH reduction

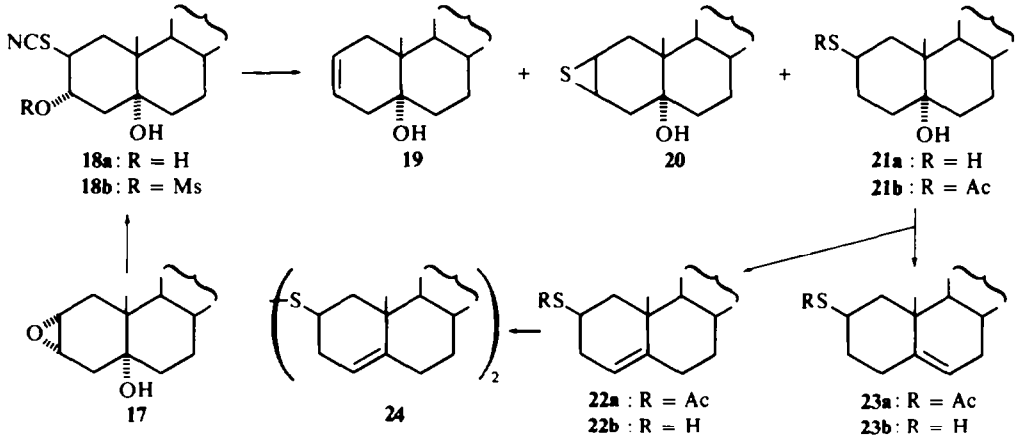
TABLE 2. RATIO OF EPIMERIC ALCOHOLS IN REDUCTION OF 3-OXO-5α-CHOLESTAN-2α,5-EPISULPHIDE (15)

| Metal hydride | 3α-*exo* alcohol (%) | | 3β-*endo* alcohol (%) | | *exo/endo* | |
|---|---|---|---|---|---|---|
| | VPC | TLC | VPC | TLC | VPC | TLC |
| $LiAlH_4$[a] | 66·5 | 66·5 | 19·9 | 10·0 | 3·34 | 6·65 |
| $NaBH_4$[b] | 75·3 | 73·5 | 22·8 | 15·5 | 3·30 | 5·44 |
| $LiAl(O_tBu)_3H$[c] | 56·3 | 47·3 | 39·4 | 35·2 | 1·43 | 1·34 |

[a] in ether; [b] in MeOH and THF; [c] in THF.

of 3-oxo-5α-cholestan-2α,5-epoxide gave exclusively a 3β-*endo* alcohol[1] in a manner similar to that observed in norcamphor,[18] the present reduction furnished the 3α-*exo* alcohol (**16a**) predominantly over the 3β-*endo* alcohol (**14c**). This fact may be ascribed to an apocamphor type reduction[18] due to the bulkiness of the bridged sulphur. However, it seems more likely that the *endo* attack by the reagent is favoured owing to the interaction between the CO group and the bridged sulphur. As can be seen in Table 2, the decrease in the ratio of the *exo/endo* alcohol in lithium aluminum tri(t.-butoxy)-hydride (bulky hydride) reduction suggests that the steric compression, newly introduced between the angular 10-Me group and the reagent in the *endo* side, operates significantly.

In addition, we studied the generality of lead tetraacetate oxidation of a homoallyl thiol leading to an *endo* acetoxy-7-thiabicyclo[2.2.1]heptane system. We chose cholest-4-ene-2β-thiol (**22b**) as the substrate. This compound was prepared from




2β-thiocyanato-5α-cholestane-3α,5-diol (**18a**),[2] derived from 5-hydroxy-5α-cholestan-2α,3α-epoxide (**17**),[2] by a 5 step sequence as follows. LAH reduction of the thiocyanato-hydrin mesylate (**18b**), obtained by the mesylation of **18a**, afforded 5α-cholest-2-en-5-ol (**19**), 5-hydroxy-5α-cholestan-2β,3β-episulphide (**20**)[2] and the desired 5-hydroxy-5α-cholestan-2β-thiol (**21a**) in 13·6%, 16·3% and 58·5% yield respectively. These were readily separated by preparative TLC. The acetylation of **21a** with pyridine and

acetic anhydride gave the 2-monoacetate (**21b**). Both **21a** and **21b** were characterized by their NMR and IR spectra. The dehydration of **21b** with thionyl chloride in pyridine afforded approximately equal amounts of an oily enethiol acetate (**22a**) and a crystalline one (**23a**). Reductive hydrolysis of both **22a** and **23a** with LAH furnished again an amorphous enethiol (**22b**) and a crystalline one (**23b**), respectively. The location of the double bond in the two pairs of compounds was deduced by calculation of the molecular rotations (Table 3). The observed values are in reasonable agreement

TABLE 3. CALCULATED MOLECULAR ROTATIONS ($M_D$)[a] OF ENETHIOLS AND ENETHIOL ACETATES

| Compd. | $M_D$ | | Assigned structure |
|---|---|---|---|
| | Found | Calcd | |
| **22b** | +315 | +261 | 4-ene-2β-thiol |
| **23b** | −190 | −231 | 5-ene-2β-thiol |
| **23a** | −172 | −281 | 5-ene-2β-thiol acetate |

[a] These $M_D$ were calculated, using the following $\Delta M_D$: 2β-SH, −24; 2β-SAc, −74 (ref 19); $\Delta^4$, +194; $\Delta^5$, −298 (ref 20).

with those calculated for the assigned structures. Furthermore, the 5-ene structure assigned to the crystalline enethiol (**23b**) was supported by its CD curve, in which a negative Cotton effect at 240 mμ and a strong positive Cotton effect at 200 mμ were observed. That the former effect corresponds to the thiol moiety is obvious from the fact that the negative Cotton effect at 230 mμ was observed in the CD curve of 5-hydroxy-5α-cholestane-2β-thiol (**21a**). Hence, the positive Cotton effect at 200 mμ suggests the presence of a $C_5$—$C_6$ double bond, in harmony with the reported data of the CD curves of steroidal olefins.[21]

Cholest-4-ene-2β-thiol (**22b**) was subjected to oxidation with lead tetraacetate in boiling cyclohexane, whereby cholest-4-en-2β-yl disulphide (**24**) was isolated as a sole crystalline product in good yield and not the expected 4α-acetoxy 5β-cholestan-2β,5-episulphide. This result may be attributable to the unfavourable orientations of the double bond and the thiol moiety in the molecule, caused by the deformation of the ring A owing to the steric compression between the 10-Me group and the thiol group disposed in a 1,3-diaxial relationship. Hence, lead tetraacetate oxidation of a homoallyl thiol, leading to *endo*-acetoxy-7-thiabicyclo[2.2.1]heptane system, would be limited to compounds possessing not only a rigid conformation but also a thiol moiety which shows resistance to dimerization.

## EXPERIMENTAL

All m.ps were measured on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were determined in 1% EtOH–$CHCl_3$ with a Perkin–Elmer Polarimeter, type 141. Unless otherwise stated, UV spectra were recorded in 95% EtOH with a Hitachi EPS-2 spectrophotometer and IR spectra in Nujol mulls by use of a Koken DS-201B spectrophotometer. NMR spectra were taken on $CDCl_3$ solns with a Varian A-60 spectrometer, TMS serving as internal standard. For preparative TLC silica gel G (E. Merck Co.) was used as an adsorbent.

*5-Acetylthio-5α-cholestan-3β-ol* (3)

A soln of 500 mg of **2** in 60 ml MeOH containing 1·5 ml 36% HCl was stirred at room temp for 28 hr. The mixture was poured into ice water and extracted with $CH_2Cl_2$. The $CH_2Cl_2$ layer was separated,

washed with $Na_2CO_3$ aq and water, and dried over $Na_2SO_4$. After evaporation of the solvent the residue was recrystallized from MeOH affording 446 mg (97%) of **3** as colorless crystals. M.p. 171–172°, $[\alpha]_D^{23}$ +48·9 ± 0·9° (*c* 0·980), $\nu_{max}$ 3231 (OH), 1682, 1110 (SAc) $cm^{-1}$. (Found: C, 75·29; H, 11·03; S, 6·89. $C_{29}H_{50}O_2S$ requires: C, 75·26; H, 10·89; S, 6·93%).

3β-*Bromo*-5α-*cholestane*-5-*thiol acetate* (**5a**)

To a cooled soln of 93 mg (0·20 mM) of **3** in 6 ml benzene was added 0·1 ml (1·05 mM) $PBr_3$. The resulting mixture was heated under reflux for 1·5 hr. After usual work up, recrystallization from MeOH gave 105 mg (quantitative yield) of **5a**, m.p. 136–137°, $[\alpha]_D^{23}$ +35·5 ± 0·7° (*c* 1·060), $\nu_{max}$ 1689, 1104 (SAc) $cm^{-1}$, $\lambda_{max}$ 236·5 mμ (ε 5000), NMR (τ): 9·36 (s, 13-Me), 8·92 (s, 10-Me), 7·74 (s, SAc), 5·33 (m, $W_{h/2}$ = 25 Hz, 3α-H). (Found: C, 66·46; H, 9·40; Br, 15·38. $C_{29}H_{49}OBrS$ requires: C, 66·36; H, 9·41; Br, 15·07%).

5-*Acetylthio*-5α-*cholestan*-3β-*ol mesylate* (**5b**)

To a cooled soln of 100 mg of **3** in 10 ml pyridine was added 0·5 ml MsCl. The mixture was allowed to stand overnight at 0°, poured into ice water, and extracted with ether. The ethereal soln was washed successively with 10% HCl, 10% $Na_2CO_3$ aq, and water, and dried over $Na_2SO_4$. After removal of the solvent, recrystallization of the residue from ether–light petroleum afforded 111 mg (95%) of **5b**, m.p. 108–110°, $[\alpha]_D^{24}$ +17·8 ± 2·1° (*c* 0·274), $\nu_{max}$ 1693, 1110 (SAc), 1356, 1163, 860 (OMs) $cm^{-1}$. (Found: C, 66·84; H, 9·72; S, 12·11. $C_{30}H_{52}O_4S_2$ requires: C, 66·62; H, 9·69; S, 11·86%).

3α-*Acetoxy*-5α-*cholestane*-5-*thiol* (**8**)

(a) *From* **5a**. A soln of 50 mg of **5a** in 5 ml collidine was heated at 130° for 2 hr. After cooling, the mixture was poured into iced 10% HCl. The deposited solid was collected by filtration and recrystallization from MeOH gave 38 mg (95%) of **8**, m.p. 151–153°, $[\alpha]_D^{23}$ +1·2 ± 0·3° (*c* 0·548), $\nu_{max}$ 2610 (SH), 1738, 1266, 1236 (OAc) $cm^{-1}$, NMR (τ): 9·35 (s, 13-Me), 9·01 (s, 10-Me), 7·93 (s, OAc), 7·47 (s, SH), 4·92 (m, $W_{h/2}$ = 9 Hz, 3β-H). (Found: C, 75·24; H, 10·96; S, 7·23. $C_{29}H_{50}O_2S$ requires: C, 75·26; H, 10·89; S, 6·93%).

(b) *From* **5b**. A soln of 140 mg of **5b** in 10 ml collidine was heated at 120° for 5 min. Work up in the same manner as described above afforded 100 mg (83·4%) of **8**.

(c) *From* **6**. The thiolacetonium perchlorate (**6**) (60 mg) was dissolved in 4 ml AcOH and the mixture was allowed to stand at room temp for 10 min. Work-up in the usual way gave 40 mg of the product which was purified by preparative TLC using cyclohexane–AcOEt (4:1) as developing solvent. The more mobile fraction yielded 35 mg (68·5%) of **8** as the pure crystals. The less mobile fraction gave 5 mg (9·8%) of **9**. The isolated minor component showed 2 spots corresponding to **8** and **9** on the TLC plate.

In another run, shaking of a soln of **6** in $CH_2Cl_2$ with $NaHCO_3$ aq or 2% $H_2SO_4$ aq for 1 min afforded a quantitative yield of **8** alone.

5α-*Cholestan*-3α-*O*, 5-*S*-*thiol acetonium perchlorate* (**6**)

To a cooled soln of 450 mg of **3** in 2 ml $CH_2Cl_2$ were added 0·1 ml conc $H_2SO_4$ and 5 ml $Ac_2O$. After shaking for 2 min, 0·19 ml 70% $HClO_4$ was added to the mixture. After addition of 100 ml dry ether, the deposited solid was collected by filtration and washed with dry ether to afford 422 mg (79·6%) of **6** as colorless crystals, m.p. 178–180° (dec.), $[\alpha]_D^{24}$ +44·0 ± 0·8° (*c* 0·452), $\nu_{max}$ 1087, 1078 ($\ominus ClO_4$) $cm^{-1}$, NMR (τ): 9·35 (s, 13-Me), 8·85 (s, 10-Me), 7·03 (s, acetonium-Me), 4·17 (m, $W_{h/2}$ = 12 Hz, 3β-H). (Found: C, 64·03; H, 9·27; Cl, 6·32; S, 6·07. $C_{29}H_{49}O_5ClS$ requires: C, 63·88; H, 9·06; Cl, 6·50; S, 5·88%).

Aqueous $Na_2CO_3$ was added to the combined filtrate and the product extracted with ether. Usual work-up gave 80 mg of a mixture exhibiting 3-spots on TLC plate. This was readily separated by preparative TLC, using cyclohexane–AcOEt (4:1) as developing solvent. In order of their decreasing mobility, the fractions yielded, 8 mg (1·8%) of **4**, m.p. 167–169°, 2 mg (0·4%) of **8**, m.p. 151–153°, and 42 mg (8·6%) of **2**, m.p. 143–144°, respectively, identified by their IR spectra.

3α-*Hydroxy*-5α-*cholestane*-5-*thiol* (**10a**)

Treatment of 98 mg (0·21 mM) of **8** with 26 mg (0·69 mM) LAH in 2 ml dry ether at 0° for 1 hr afforded the product, which was recrystallized from MeOH to give 88 mg (quantitative yield) of **10a**, m.p. 128–131°, $[\alpha]_D^{23}$ −2·1 ± 0·8° (*c* 0·531), $\nu_{max}$ 3294 (OH), 2564 (SH) $cm^{-1}$, NMR (τ): 9·35 (s, 13-Me), 9·02 (s, 10-Me), 5·93 (m, $W_{h/2}$ = 8 Hz, 3β-H). (Found: C, 76·77; H, 11·28; S, 7·45. $C_{27}H_{48}OS$ requires: C, 77·06; H, 11·50; S, 7·62%).

3α-*Hydroxy*-5α-*cholestane*-5-*thiol* 3,5-*diacetate* (**10b**)

Treatment of 54 mg of **10a** with 3 ml $Ac_2O$ in 3 ml pyridine for 2 days at room temp gave 57 mg of an oily product which was subjected to preparative TLC using cyclohexane–AcOEt (4:1) as developing solvent. The more mobile fraction afforded 4 mg of **8**, which was identified by the IR spectrum. The less mobile fraction furnished **10b**, which was recrystallized from MeOH yielding 26 mg (44·4%) of pure **10b**, m.p.

202–203°, $[\alpha]_D^{24}$ −8·5 ± 1·4° (*c* 0·340), $\nu_{max}$ 1729, 1268, 1249, 1230 (OAc), 1672, 1114 (SAc) $cm^{-1}$, $\lambda_{max}$ 240 mμ (ε 5100). (Found: C, 73·93; H, 10·34; S, 6·62. $C_{31}H_{52}O_3S$ requires: C, 73·76; H, 10·38; S, 6·35%).

*5-Thiocyanato-5α-cholest-2-en-6β-ol* (**12a**)

To a mixture of 20 g KSCN dissolved in a small volume ice water and 30 ml ether, was added 15 g $H_3PO_4$ in small portions and the mixture was shaken to extract the HSCN formed into the ethereal layer. The pink-colored HSCN-ether soln was dried over $Na_2SO_4$ and added to a soln of 5·2 g of **11** in 20 ml ether. The mixture was allowed to stand at room temp for 1 hr, washed with 10% $Na_2CO_3$ aq and water, dried, and evaporated to dryness under reduced press. Recrystallization from ether–light petroleum gave 6·1 g of **12a**, m.p. 157–159°, $[\alpha]_D^{24}$ −20·0 ± 0·9° (*c* 0·695), $\nu_{max}$ 3473, 1050 (OH), 3045, 1658, 675 (Δ2), 2160 (SCN) $cm^{-1}$, NMR (τ): 9·32 (s, 13-Me), 8·79 (s, 10-Me), 5·85 (m, $W_{h/2}$ = 6 Hz, 6α-H), 4·29 (m, 2-H, 3-H). (Found: C, 75·58; H, 10·17; N, 3·44; S, 7·57. $C_{28}H_{45}NOS$ requires: C, 75·79; H, 10·22; N, 3·16; S, 7·23%).

*5α-Cholest-2-ene-5-thiol* (**1a**)

Treatment of 6·1 g of **12a** with 6·0 g MsCl in 90 ml pyridine at room temp overnight afforded 6·5 g of **12b** as an oily material, $\nu_{max}^{CCl_4}$ 3030, 1665 (Δ²), 2200 (SCN), 1340, 1178, 1115, 890 (OMs) $cm^{-1}$.

To a stirred suspension of 3·06 g LAH in 20 ml dry ether was added a soln of 6·5 g of **12b** obtained above in 60 ml of a mixture of dry ether and THF (1:1). The mixture was heated under reflux with stirring for 2 hr and worked up in the usual way to afford 4·0 g of a solid. The crude product was purified by chromatography over 80 g of Florisil. The eluates with light petroleum was further recrystallized from acetone affording 3·2 g (58·2% from **11**) of **1a** as colorless crystals, m.p. 109·5–110·5°, $[\alpha]_D^{25}$ +179·0 ± 2·0° (*c* 0·821), $\nu_{max}$ 3025, 1650, 665 (Δ²) $cm^{-1}$, NMR (τ): 9·35 (s, 13-Me), 9·10 (s, 10-Me), 4·37 (m, 2-H, 3-H). (Found: C, 80·59; H, 11·48; S, 7·89. $C_{27}H_{46}S$ requires: C, 80·52; H, 11·51; S, 7·96%).

*5α-Cholest-2-ene-5-thiol acetate* (**1b**)

Treatment of 200 mg of **1a** with 2 ml pyridine and 1 ml $Ac_2O$ at room temp overnight afforded a mixture of **1a** and **1b**. The mixture was separated by preparative TLC, using cyclohexene–AcOEt (99:1) as developing solvent. The more mobile fraction gave 34 mg (17%) of the starting material (**1a**). The less mobile fraction was recrystallized from ether–MeOH to yield 148 mg (67%) of **1b**, m.p. 100–100·5°, $[\alpha]_D^{24}$ +46·2 ± 0·8° (*c* 1·017), $\nu_{max}^{CCl_4}$ 3016, 1641, 675 (Δ²), 1679, 1110, 949 (SAc) $cm^{-1}$, $\lambda_{max}^{isooctane}$ 234·5 mμ (ε 5400), NMR (τ): 9·35 (s, 13-Me), 9·09 (s, 10-Me), 7·78 (s, SAc), 4·38 (m, 2H, 3H). (Found: C, 78·61; H, 10·84; S, 7·44. $C_{29}H_{48}OS$ requires: C, 78·31; H, 10·88; S, 7·21%).

*3β-Bromo-5α-cholestan-2α,5-episulphide* (**13a**)

To a cooled soln of 3·0 g (7·46 mM) of **1a** in 30 ml $CCl_4$ a soln of 1·23 g (7·69 mM) $Br_2$ in 10 ml $CCl_4$ was added dropwise, with stirring, during 1 hr. The mixture was stirred for an additional 1 hr at room temp and concentrated under reduced press at less than 30°. The orange residual oil was dissolved in ether and filtered through active carbon to decolorize. After evaporation of the ether, the resulting yellow solid was recrystallized from acetone to give 3·35 g (92%) of **13a** as colorless crystals, m.p. 88–89°, $[\alpha]_D^{24}$ +43·1 ± 1·3° (*c* 0·620), $\nu_{max}$ 1306, 1236, 1160, 1153, 1140, 962, 855 $cm^{-1}$, $\lambda_{max}^{isooctane}$ 261, 216·5, 203·5 mμ (ε 180, 2210, 1800), NMR (τ): 9·33 (s, 13-Me), 8·92 (s, 10-Me), 6·41 (t, *J* = 4·0 Hz, 2β-H), 5·40 (m, 3α-H), 100 MHz-NMR (τ): 8·160 (1α-H), 7·804 (1β-H), 6·383 (2β-H), 5·391 (3α-H), *ca* 2·27 (4α-H, 4β-H). $J_{1\alpha:1\beta}$ = −13·0, $J_{4\alpha:4\beta}$ = −14·0, $J_{1\alpha:2\beta}$ = 4·0, $J_{1\beta:2\beta}$ = 0·7, $J_{2\beta:3\alpha}$ = 4·0, $J_{3\alpha:4\alpha}$ = 9·5, $J_{3\alpha:4\beta}$ = 4·0, $J_{1\alpha:3\alpha}$ = 2·0 Hz. (Found: C, 67·34; H, 9·44; Br, 16·77; S, 6·62. $C_{27}H_{45}BrS$ requires: C, 67·33; H, 9·42; Br, 16·59; S, 6·66%).

*3β-Chloro-5α-cholestan-2α,5-episulphide* (**13b**)

(a) 5α-Cholest-2-ene-5-thiol (**1a**; 700 mg) was treated with a soln of 141 mg of $Cl_2$ in 8 ml $CCl_4$ as described. Recrystallization of the product from acetone gave 431 mg (57%) of **13b**, m.p. 69–70°, $[\alpha]_D^{23}$ +11·1 ± 0·7° (*c* 0·709), $\nu_{max}$ 1306, 1252, 1212, 1168, 1152, 962, 855 $cm^{-1}$, NMR (τ): 9·34 (s, 13-Me), 8·92 (s, 10-Me), 6·44 (t, *J* = 4·0 Hz, 2β-H), 5·44 (m, 3α-H). (Found: C, 74·12; H, 10·34; Cl, 8·30; S, 7·35. $C_{27}H_{45}ClS$ requires: C, 74·18; H, 10·38; Cl, 8·11; S, 7·34%).

(b) To a cooled soln of 150 mg of **14c** in 3 ml pyridine was added 0·15 ml MsCl portionwise. The pink colored mixture was allowed to stand at 15° for 3·5 hr and worked up in the usual way. The neutral fraction extracted with ether gave only 30 mg of an oily product, which was purified by recrystallization from acetone to yield 15 mg of **13b**, m.p. 69–70°, identified by mixed m.p. and comparison of the IR spectrum.

*5α-Cholestan-2α,5-episulphide* (**13c**)

(a) Reduction of 200 mg of **13a** with 62 mg LAH in 5 ml of dry ether at room temp overnight afforded a mixture, showing 3 spots on TLC plate. The mixture was subjected to preparative TLC, using cyclohexane–AcOEt (8:1) as developing solvent. The more mobile fraction gave 17 mg (10·2%) of **1a**. The less mobile fraction was recrystallized from acetone to yield 36 mg (21·6%) of **13c**, m.p. 58–59°, $[\alpha]_D^{24}$ −1·6 ± 1·1° (*c* 0·370), $\nu_{max}$ 1308, 1219, 955, 935, 910, 856, 793 $cm^{-1}$, $\lambda_{max}^{isooctane}$ 257 mμ (ε 30), NMR (τ): 9·33 (s, 13-Me),

9·05 (s, 10-Me), 6·37 (t, $J$ = 3·5 Hz, 2β-H). (Found: C, 80·72; H, 11·39; S, 8·09. $C_{27}H_{46}S$ requires: C, 80·53; H, 11·51; S, 7·96%). The least mobile fraction yielded 50 mg (30%) of a mixture, which was not further studied.

(b) A mixture of 3·0 g (6·23 mM) of **13a** and 2·4 g (63·2 mM) $NaBH_4$ in 60 ml DMF was heated at 50° with stirring for 2 hr. Usual work-up afforded 2·46 g of an oily product, which was chromatographed over 75 g of standardized $Al_2O_3$ (grade II). The fraction eluted with light petroleum gave a crystalline solid, which was recrystallized from acetone to afford 2·19 g (87·5%) of **13c**, m.p. 58–59°.

*The reaction of* 3β-*bromo*-5α-*cholestan*-2α,5-*episulphide* (**13a**) *with potassium acetate*

A stirred mixture of 520 mg (1·08 mM) of **13a** and 400 mg (4·0 mM) KOAc in 12 ml DMF was heated at 110° for 2 hr and worked up in the usual way to yield 482 mg of an oily product, exhibiting 3 spots on TLC plate. The mixture was submitted to preparative TLC using cyclohexane–AcOEt (1 : 1) as developing solvent. The most mobile fraction was recrystallized from MeOH to give 26 mg (5·4%) of **14b**, m.p. 97·5–99°, $[\alpha]_D^{23}$ +2·0 ± 1·7° (*c* 0·252), $\nu_{max}$ 1730, 1191, 1169, 995 (OCHO) $cm^{-1}$, $\lambda_{max}^{isooctane}$ 255, 204 mμ (ε 60, 3400), NMR (τ): 9·33 (s, 13-Me), 8·97 (s, 10-Me), 6·33 (m, 2β-H), 4·69 (m, 3α-H). (Found: C, 75·32; H, 10·39. $C_{28}H_{46}O_2S$ requires: C, 75·28; H, 10·38%). The middle fraction was recrystallized from acetone to give 352 mg (71%) of **14a**, m.p. 120·5–121°, $[\alpha]_D^{23}$ +3·5 ± 0·7° (*c* 0·600), $\nu_{max}$ 1755, 1245, 1034, 1020, 999 (OAc), 921 $cm^{-1}$, $\lambda_{max}^{isooctane}$ 258, 204·5 mμ (ε 41, 2810), NMR (τ): 9·33 (s, 13-Me), 8·97 (s, 10-Me), 7·96 (s, OAc), 6·33 (t, d; $J$ = 4·0, 2·0 Hz; 2β-H), 4·80 (t, d; $J$ = 4·0, 8·0 Hz; 3α-H). (Found: C, 75·45; H, 10·52; S, 7·15. $C_{29}H_{48}O_2S$ requires: C, 75·59; H, 10·50; S, 6·96%). The least mobile fraction was recrystallized from MeOH affording 88 mg (19·5%) of **14c**, m.p. 149–150°, $[\alpha]_D^{22}$ −3·9 ± 0·5° (*c* 0·933), $\nu_{max}$ 3467, 3273, 1050, 1020 (OH) $cm^{-1}$, NMR (τ): 9·33 (s, 13-Me), 8·93 (s, 10-Me), 8·31 (s, OH), 6·64 (t, $J$ = 3·5 Hz, 2β-H), 5·45 (d, t; $J$ = 7·0, 3·5 Hz; 3α-H). (Found: C, 77·01; H, 11·06; S, 7·65. $C_{27}H_{46}OS$ requires: C, 77·45; H, 11·07; S, 7·66%).

(a) Reduction of **14a** or **14b** with 2 molar equivts LAH in dry ether for 30 min at room temp gave in *ca* 91% of **14c**.

(b) Acetylation of **14c** with pyridine and $Ac_2O$ in the usual way afforded **14b** in quantitative yield.

(c) Thus, 985 mg of **13a** was treated with 800 mg KOAc in 24 ml DMF in the same manner as described and reduction of the product with 152 mg LAH in 20 ml ether afforded 730 mg (85·5%) of **14c**.

3β-*Methoxy*-5α-*cholestan*-2α,5-*episulphide* (**14d**)

A soln of 100 mg of **13a** in 3 ml MeOH was allowed to stand overnight at room temp. After evaporation of the solvent under reduced press, recrystallization from acetone yielded 77 mg (85·5%) of **14d**, m.p. 88–89°, $[\alpha]_D^{23}$ −2·5 ± 2·6° (*c* 0·159), $\nu_{max}$ 1095 (OMe) $cm^{-1}$, NMR (τ): 9·33 (s, 13-Me), 8·97 (s, 10-Me), 6·72 (s, OMe), 6·44 (t, $J$ = 3·3 Hz, 2β-H), 6·03 (m, 3α-H). (Found: C, 77·77; H, 11·06; S, 7·64. $C_{28}H_{48}OS$ requires: C, 77·71; H, 11·18; S, 7·41%).

*The reaction of* 5α-*cholest*-2-*ene*-5-*thiol* (**1a**) *with lead tetraacetate*

A mixture of 23·8 g (53·8 mM) $Pb(OAc)_4$ and 7·6 g (76 mM) $CaCO_3$ in 300 ml cyclohexane was heated under reflux with stirring for 1 hr. To the boiled mixture a soln of 5·4 g (13·4 mM) of **1a** in 50 ml cyclohexane was added dropwise. After refluxing for 5 min, the reaction mixture was filtered to remove the excess reagent. The filtrate was diluted with ether. The soln was washed with 10% $Na_2CO_3$aq and water and dried over $Na_2SO_4$. After removal of the solvent under reduced press, 6·0 g of the resulting solid was recrystallized from acetone, affording 5·3 g (86%) of **14a** as colorless crystals, m.p. 120·5–121°, which was identified by mixed m.p. and comparison of the IR spectrum.

3-*Oxo*-5α-*cholestan*-2α,5-*episulphide* (**15**)

A soln of 1·302 g (3·11 mM) of **14c** in a mixture of 6·5 ml (62·3 mM) cyclohexanone and 52 ml dry toluene was distilled to give 5 ml distillate. Then slow distillation was continued while a soln of 650 mg (3·19 mM) Al(i-PrO)$_3$ in 18 ml dry toluene was added dropwise over a period of 20 min. After slow distillation for an additional 40 min, giving 20 ml total distillate, a soln of Rochelle salt in water was added to the cooled mixture which was then extracted with ether. Usual work-up afforded 1·213 g of the product, which was chromatographed over 35 g neutral $Al_2O_3$ (grade II). The fraction eluted with light petroleum yielded a small amount of an oily substance. The fractions eluted with light petroleum–benzene (5:1 ~ 3:2) were combined and recrystallized from ether–MeOH giving 1·062 g (81%) of **15**, m.p. 103–103·5°, $[\alpha]_D^{24}$ −171·0 ± 2·0° (*c* 0·294), $\nu_{max}$ 1753 (CO), 1415 (active $CH_2$), 1202, 1190, 956 $cm^{-1}$, NMR (τ): 9·32 (s, 13-Me), 9·00 (s, 10-Me), 6·40 (d, $J$ = 5·0 Hz, 2β-H). (Found: C, 78·04; H, 10·66; S, 7·79. $C_{27}H_{44}OS$ requires: C, 77·82; H, 10·64; S, 7·70%).

3α-*Hydroxy*-5α-*cholestan*-2α,5-*episulphide* (**16a**)

The ketone **15** (200 mg, 0·48 mM) was treated with 5·0 mg (1·33 mM) $NaBH_4$ in 5 ml of a mixture of MeOH and THF (1 : 7) for 1 hr at room temp. Usual work-up gave 205 mg of a mixture of epimeric alcohols,

(**14c** and **16a**). These were separated by preparative TLC (cyclohexane–AcOEt = 15:1) using an infinite developing method (for 4 hr). The more mobile fraction gave 32 mg (16%) of **14c**, m.p. 149–150°. The less mobile fraction afforded 140 mg (70%) of **16a**, which was recrystallized from acetone yielding the pure sample, m.p. 163·5–164·5°, $[\alpha]_D^{23}$ −13·0 ± 1·1° (*c* 0·477), $\nu_{max}$ 3432, 1052 (OH), $cm^{-1}$, NMR (τ): 9·33 (s, 13-Me), 9·09 (s, 10-Me), 6·55 (d, *J* = 5·0 Hz, 2β-H), 6·06 (m, 3β-H). (Found: C, 77·62; H, 11·09; S, 7·59. $C_{27}H_{46}OS$ requires: C, 77·45; H, 11·07; S, 7·66%).

*3α-Acetoxy-5α-cholestan-2α,5-episulphide* (**16b**)

Treatment of **16a** with $Ac_2O$ and pyridine at room temp overnight afforded in good yield **16b**, which was recrystallized from acetone, m.p. 129·5–130·5, $[\alpha]_D^{23}$ −30·7 ± 1·4° (*c* 0·505), $\nu_{max}$ 1732, 1275, 1036 (OAc) $cm^{-1}$, NMR (τ): 9·33 (s, 13-Me), 9·09 (s, 10-Me), 7·94 (s, OAc), 6·42 (d, *J* = 4·0 Hz, 2β-H), 5·13 (q, *J* = 7·0, 3·0 Hz; 3β-H). (Found: C, 75·78; H, 10·47; S, 7·02. $C_{29}H_{48}O_2S$ requires: C, 75·59; H, 10·50; S, 6·96%).

*3α-Mesyloxy-5α-cholestan-2α,5-episulphide* (**16c**)

To a cooled soln of 607 mg of **16a** in 15 ml pyridine was added 0·6 ml MsCl. The resulting mixture was allowed to stand at room temp overnight. After work-up in the usual way, recrystallization from MeOH afforded 652 mg (90·3%) of **16c**, m.p. 120–121·5°, $[\alpha]_D^{21}$ −24·9 ± 1·4° (*c* 0·445), $\nu_{max}$ 1338, 1175, 997, 985, 966 (OMs) $cm^{-1}$, $\lambda_{max}^{isooctane}$ 255, 205 mμ (ε 134, 2000), NMR (τ): 9·34 (s, 13-Me), 9·11 (s, 10-Me), 6·98 (s, OMs), 6·24 (d, *J* = 4·5 Hz, 2β-H), 5·10 (q; *J* = 6·5, 3·5 Hz; 3β-H). (Found: C, 67·46; H, 9·67; S, 12·81. $C_{28}H_{48}O_3S_2$ requires: C, 67·69; H, 9·74; S, 12·91%).

*Gas-chromatographic analyses of the reduction products of 3-oxo-5α-cholestan-2α,5-episulphide* (**15**)

Analyses were carried out with Model Shimadzu GC 4APTF (FID) using 1·5 m × 4 mm glass column packed with 1% cyclohexane dimethanol succinate polyester (HCl, silanized, 100/120 mesh), $N_2$ as carrier gas and cholestanol as internal standard under the following conditions: column temp, 253·2°; injector temp, 255·0°; detector temp, 261·2°, retention time: cholestanol, 8·0 min; 3β-*endo* alcohol (**17c**), 17·0 min; 3α-*exo* alcohol (**19a**), 23·7 min (flow rate of $N_2$, 46·1 cc/min).

A mixture of epimeric alcohols, obtained in the reduction of **15** with three metal hydrides in the presence of cholestanol, was trimethyl sililated with N,O-bis(trimethylsilyl)acetamide at room temp and analyzed.

*Preparative TLC analyses of the reduction products of 3-oxo-5α-cholestan-2α,5-episulphide* (**15**)

A mixture of epimeric alcohols obtained by reduction of **15**, was acetylated with $Ac_2O$-pyridine at room temp overnight. After work-up in the usual way, the mixture of **14a** and **16b** were separated into each component by preparative TLC (benzene–cyclohexane = 1:1) and weighed.

*2β-Thiocyanato-3α-mesyloxy-5α-cholestan-5-ol* (**18b**)

To a cooled soln of 2·2 g of **18a**[2] in 22 ml pyridine was added 0·22 ml MsCl. The resulting mixture was allowed to stand at room temp overnight, then poured into ice water, and extracted with ether. Usual work-up gave 2·47 g (96%) of **18b** as an oily material, $\nu_{max}^{CCl_4}$ 3580, 3500 (OH), 2180 (SCN), 1178 (OMs) $cm^{-1}$.

*5-Hydroxy-5α-cholestane-2β-thiol* (**21a**)

To a cooled suspension of 900 mg (23·7 mM) LAH in 20 ml of a mixture of ether and THF (1:1) was added a soln of 2·47 g (4·57 mM) of **18b** in 50 ml of the same solvent at 0°. The reaction mixture was stirred at 0° for 2 hr and worked up in the usual way to give 1·85 g of the product, which showed 3 spots on TLC plate. The mixture was submitted to chromatography over 180 g of $SiO_2$, using cyclohexane–AcOEt (9:1) as elution solvent. The first fraction eluted with 120 ml of the solvent gave 240 mg (13·6%) of **19**, m.p. 93–95°, which was identified by mixed m.p. and comparison of the IR spectrum. The second fraction eluted with 300 ml of the solvent afforded 1·12 g (58·5%) of **21a**, which was recrystallized from acetone to give the pure sample, m.p. 116–117°, $[\alpha]_D^{24}$ +5·1 ± 0·5° (*c* 0·954), $\nu_{max}^{CCl_4}$ 3580 (OH), 920 $cm^{-1}$, CD* (in isooctane): $[\theta]_{230}$ −3070, NMR (τ): 9·33 (s, 13-Me), 8·77 (s, 10-Me), 6·33 (m, $W_{h/2}$ = 12 Hz, 2α-H). (Found: C, 77·28; H, 11·46; S, 7·51. $C_{27}H_{48}OS$ requires: C, 77·08; H, 11·50; S, 7·62%). The third fraction eluted with 200 ml of the solvent gave 310 mg (16·3%) of **20**,[2] m.p. 105–107°, which was identified by mixed m.p. and comparison of the IR spectrum.

*2β-Acetylthio-5α-cholestan-5-ol* (**21b**)

The thiol **21a** (860 mg) was acetylated with 4·5 ml $Ac_2O$ and 9 ml pyridine at room temp overnight. Recrystallization of the product from acetone yielded 930 mg (98·5%) of **21b**, m.p. 50–52°, $[\alpha]_D^{24}$ −9·4 ± 0·5° (*c* 0·984), $\nu_{max}^{CCl_4}$ 3600 (OH), 1692, 1115, 955 (SAc), 925 $cm^{-1}$, NMR (τ): 9·37 (s, 13-Me), 8·95 (s, 10-Me), 7·73 (s, SAc), 5·95 (m, $W_{h/2}$ = 12 Hz, 2α-H). (Found: C, 74·95; H, 10·79; S, 6·78. $C_{29}H_{50}O_2S$ requires: C, 75·26; H, 10·89; S, 6·93%).

* These CD curves were measured by Dr. K. Kuriyama and Mr. Iwata with a Jasco Model ORD/UV-5 equipped with CD.

*Dehydration of* 2β-*acetylthio*-5α-*cholestan*-3-*ol* (**21b**)

To a cooled soln of 930 mg (2·01 mM) of **21b** in 10 ml pyridine was added 2 ml (26·8 mM) $SOCl_2$ dropwise at 0°. The resulting mixture was allowed to stand at 0° for 1 hr and worked up to give 840 mg of an oily mixture, which exhibits 2 spots on TLC plate. The mixture was submitted to preparative TLC, using cyclohexane–AcOEt (40:1) as developing solvent. The more mobile fraction afforded 310 mg (34·4%) of **22a** as an oily substance, which could not be crystallized from any solvents. The less mobile fraction was recrystallized from acetone to give 355 mg (39·5%) of **23a** as colorless crystals, m.p. 142–143°, $[\alpha]_D^{24}$ −38·8 ± 0·8° (*c* 0·970), $\nu_{max}^{CCl_4}$ 1695, 1140, 1120, 952 (SAc) cm$^{-1}$, $\lambda_{max}^{isooctane}$ 231 mμ (ε 4760), CD (in isooctane): $[\theta]_{270}$ +2017, $[\theta]_{205}$ +20170, NMR (τ): 9·33 (s, 13-Me), 8·94 (s, 10-Me), 7·71 (s, SAc), 6·01 (m, $W_{h/2}$ = 10 Hz, 2α-H), 4·71 (m, $W_{h/2}$ = 8 Hz, 6-H). (Found: C, 78·44; H, 10·87; S, 7·10. $C_{29}H_{48}OS$ requires: C, 78·32; H, 10·87; S, 7·21%).

*Cholest*-4-*ene*-2β-*thiol* (**22b**)

The oily **22a** (420 mg) was reduced with 120 mg LAH in 7 ml dry ether for 1 hr at room temp. Usual work-up gave 380 mg (quantitative yield) of **22b** as a colorless oil, whose homogeneity was established by TLC using infinite developing method; $[\alpha]_D^{24}$ +78·4 ± 1·5° (*c* 0·790), $\nu_{max}$ 2590 (SH), 1656 ($\Delta^4$), 807 cm$^{-1}$, NMR (τ): 9·34 (s, 13-Me), 9·00 (s, 10-Me), 6·9–7·3 (m, 2α-H), 4·77 (m, $W_{h/2}$ = 10 Hz, 4H).

*Cholest*-5-*ene*-2β-*thiol* (**23b**)

The crystalline **23a** (450 mg) was reduced with 130 mg LAH in 8 ml of dry ether under the conditions as described. After work-up in the usual way, recrystallization from acetone afforded 380 mg (93·5%) of **23b** as colorless crystals, m.p. 117·5–118·5°, $[\alpha]_D^{24}$ −47·3 ± 0·9° (*c* 0·943), $\nu_{max}$ 2573 (SH), 1670 ($\Delta^5$), 960, 835, 801 cm$^{-1}$, CD* (in isooctane); $[\theta]_{240}$ −993, $[\theta]_{200}$ +32390, NMR (τ): 9·33 (s, 13-Me), 8·82 (s, 10-Me), 6·60 (m, $W_{h/2}$ = 15 Hz, 2α-H), 4·71 (m, $W_{h/2}$ = 9 Hz, 6-H). (Found: C, 80·26; H, 11·47; S, 7·62. $C_{27}H_{46}S$ requires: C, 80·52; H, 11·51; S, 7·96%).

*Bis-cholest*-4-*en*-2β-*yl disulphide* (**24**)

A stirred suspension of 265 mg (0·60 mM) $Pb(OAc)_4$ and 90 mg (0·90 mM) $CaCO_3$ in 3 ml cyclohexane was heated under reflux for 30 min. To the boiled mixture was added 60 mg (0·15 mM) of **22b** in 1 ml cyclohexane. After refluxed for 30 min with stirring, the mixture was worked up as described, affording 55 mg of a solid, which was purified by preparative TLC using cyclohexane as developing solvent. Recrystallization from acetone gave 40 mg (67%) of **24** as colorless crystals, m.p. 129–131·5°, $[\alpha]_D^{24}$ +71·6 ± 0·6° (*c* 0·899), $\nu_{max}^{CCl_4}$ 800 cm$^{-1}$, MS†: *m/e* 802 (1%) [M$^+$], *m/e* 368 (100%) [M$^+$/2 − HS]; NMR (τ): 9·32 (s, 13-Me), 8·95 (s, 10-Me), 6·9–7·3 (m, 2α-H), 4·72 (m, $W_{h/2}$ = 9·5 Hz, 4-H). (Found: C, 80·32; H, 11·18. $C_{54}H_{90}S_2$ requires: C, 80·66; S, 11·28%).

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† Mass spectrum was determined by Dr. Y. Nakagawa and Mr. H. Moriyama with a Hitachi RMU-6 mass spectrometer.

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