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BILE ACIDS AND STEROIDS—XXVII

THIOSTEROIDS (12)[1] STEROIDAL 2,3- AND 3,4-EPISULPHIDES AND RELATED COMPOUNDS*

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Abstract—Synthetic methods for, and some reactions of the steroidal 2,3- and 3,4-episulphides and related compounds are described. The five-membered ring formation, e.g. acetonide, trithiocarbonate etc., of the 2,3-*trans*-diaxial dimercapto and mercapto-ol derivatives are also studied.

IN CONNECTION with the study on the ring-opening reaction of a number of steroidal oxides by thiocyanic acid,[2] this report describes the synthesis and some reactions of 2,3- and 3,4-episulphides,[3] and also acetonide formation of the vicinal mercapto-ols.

When cholestan-2α,3α-oxide (Ia) was treated with thiocyanic acid, there was obtained the 2β-thiocyanato-3α-ol (IIa) in good yield, in which the configuration at C_2 or C_3 was anticipated to be in keeping with the Barton rule.[4] Reduction of this compound with lithium aluminum hydride gave the 2β-mercapto-3α-ol (IIIa). This assignment was established from the following chemical evidence. The thiocyanato ketone (IVa) obtained in 50% yield by oxidation of the compound (IIa) with chromium trioxide–sulphuric acid in acetone, was converted to cholestan-3-one with zinc in acetic acid in a quantitative yield. In addition, treatment of 2α-bromocholestan-3-one (V) with potassium thiocyanate in acetone afforded the same thiocyanato ketone (IVa), and this ketone showed an optical rotatory dispersion curve similar to that of cholestan-3-one. The NMR spectrum of the ketone exhibited a quartet at 5·64 τ (J = 13·0, 6·4 c/s), which was attributed to the X part of the ABX system and therefore belonging to the proton on C_2. This pattern was also observed in the spectra of both 2α-bromo- (V)[5] and 2α-ethylxanthate-cholestan-3-one (IVb).[6] These results indicate that the thiocyanato group on C_2 is equatorial and furthermore that epimerization had occurred during the oxidation step.

Reduction of this thiocyanato ketone with lithium aluminum hydride yielded the 2α-mercapto-3β-ol (VIa), identical with that obtained by similar reduction of the 2α-ethylxanthate ketone (IVb). The 2α-mercapto-3β-ol, having *trans*-diequatorial

* A part of this work was outlined in *Chem. & Ind.* 1793 (1962).

[1] Thiosteroids (11), K. Takeda, K. Igarashi and M. Narisada, *Steroids* **4**, 305 (1964).

[2a] K. Takeda and T. Komeno, *Chem. Pharm. Bull., Japan*, **8**, 468 (1960).

[2b] T. Komeno, *Ibid.* **8**, 672 (1960); [2c] T. Komeno, *Ibid.* **8**, 680 (1960).

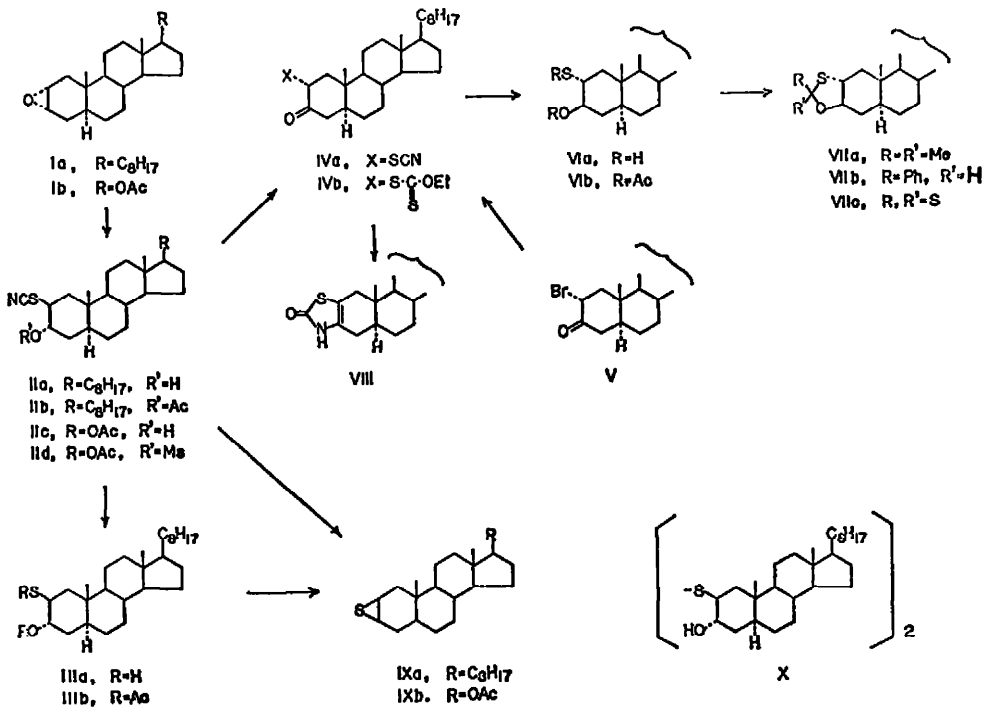
[3a] D. A. Lightner and C. Djerassi, *Chem. & Ind.* 1236 (1962);

[3b] K. Takeda and T. Komeno, *Ibid.* 1793 (1962).

[4] D. H. R. Barton, *J. Chem. Soc.* 1027 (1953).

[5] R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.* 806 (1963).

[6] C. Djerassi, M. Gorman, F. X. Markley and E. B. Oldenburg, *J. Amer. Chem. Soc.* **77**, 568 (1955).



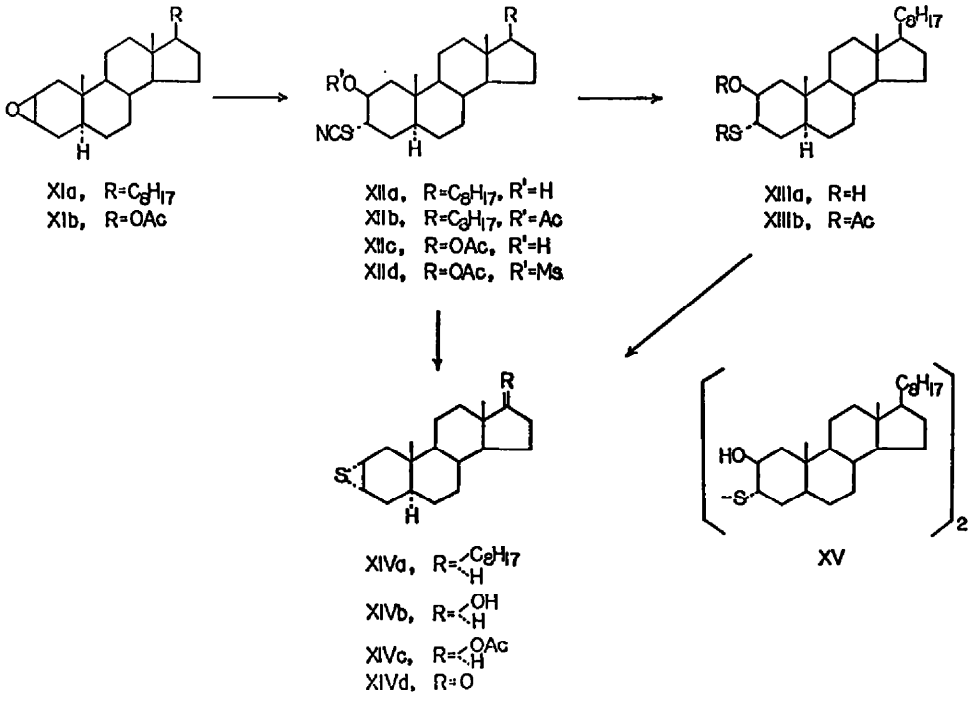
substituents, was allowed to react with acetone, benzaldehyde, or N,N'-thiocarbonyl-bis(2-methylimidazol)[7] to give a 1,3-oxathiolano derivative (VIIa, VIIb or VIIc) as mentioned by Djerassi *et al.*[6]

Cyclization of the thiocyanato ketone (IVa) was carried out by heating in dioxane containing aqueous hydrochloric acid to give an oxothiazoline (VIII) in about 50% yield. The IR spectrum of this compound showed absorption bands at 3030, 1680 and 1574 cm^{-1} due to the lactam group.

In the case of the 2β,3β-oxide (XIa), thiocyanation also proceeded smoothly and the 3α-thiocyanato-2β-ol (XIIa) was obtained in good yield. This compound was also reduced to the corresponding 3α-mercapto-2β-ol (XIIIa).

In contrast to oxide formation of the 12α-thiocyanato-11β-ol[2a] or 16β-thiocyanato-17α-ol,[2c] the action of potassium hydroxide in ethanol on the 2β-thiocyanato-3α-ol (IIa) or 2β-mercapto-3α-ol diacetate (IIIb) gave cholestan-2β,3β-episulphide (IXa) in an almost quantitative yield, while by the same treatment the free mercapto-ol (IIIa) gave 70% of the unchanged starting material accompanied by 10% of the corresponding disulphide (X). Similarly, under the same conditions both the 3α-thiocyanato-2β-ol (XIIa) and the 3α-mercapto-2β-ol diacetate (XIIIb) yielded cholestan-2α,3α-episulphide (XIVa), while the free mercapto-ol gave only the corresponding disulphide (XV) in 70% yield. The latter was confirmed by reduction to the parent mercapto-ol (XIIIa). The same treatment of the *trans*-diequatorial derivative

[7] Staab and Walther found that N,N'-thiocarbonylbisimidazol reacted with an alcohol to give a thioxocarbonate. (H. A. Staab, G. Walther, *Liebigs Ann.* **657**, 98 (1962).) Corey also used this reagent for preparation of a thioxocarbonate from a vicinal diol. (E. J. Corey, R. A. E. Winter, *J. Amer. Chem. Soc.* **85**, 2677 (1963).)



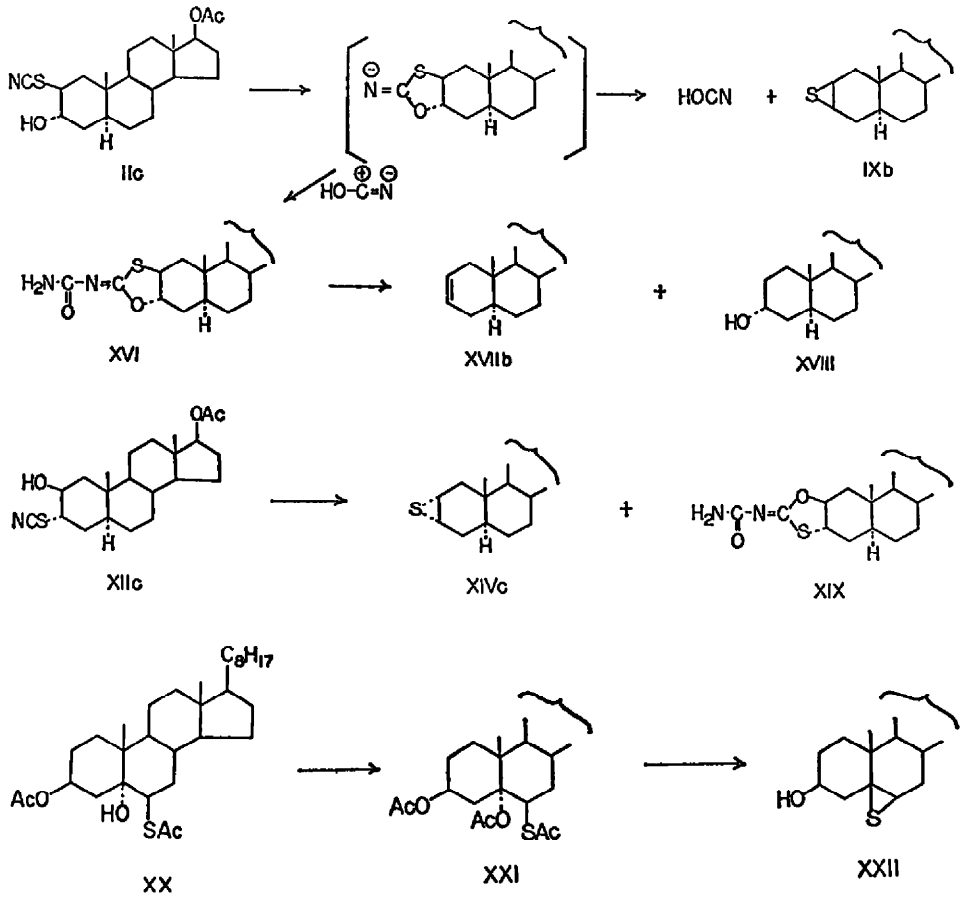
2α-mercapto-3β-ol diacetate (VIb) afforded only an intractable gel with no formation of the episulphide.

The 2α,3α- and 2β,3β-episulphide (IXb and XIVc) of 17β-acetoxy-5α-androstane were also respectively obtained from the 17β-acetoxyandrostan-2,3-oxide having the reverse configuration by treatment with thiocyanic acid, followed by alkaline treatment directly or indirectly *via* the mesylate (IId or XIId). In this case it is interesting to note that the thiocyanatoandrostanediol (IIc or XIIc) was treated with Florisil to give the episulphide and an urea derivative (XVI or XIX).[8] The structure of the urea derivative was confirmed from the IR and NMR data and furthermore from the fact that XVI was reduced with Raney nickel to give 5α-androst-2-en-17β-ol (XVII) and 5α-androstane-3α,17β-diol (XVII). These results indicated that even in the rigid steroid system the direct conversion of vicinal diaxial thiocyanato-ol to episulphide proceeds *via* van Tamelen's "cyclic intermediate"[9] and the subsequent disproportionation occurs as shown in the following chart.

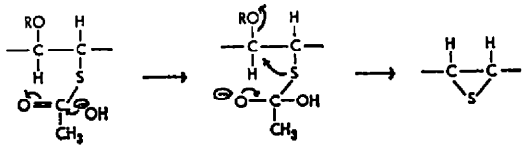
However, it is assumed that conversion of the steroidal vicinal mercapto-ol diacetate to episulphide is somewhat different from the above reaction and proceeds smoothly even when there is no possibility of a cyclic intermediate. For example, 6β-acetylthiocholestane-3β,5α-diol diacetate (XXI), prepared from 6β-acetylthiocholestane-3β,5α-diol 3-monoacetate (XX)[8b] by forced acetylation, was treated with KOH–EtOH to yield 3β-hydroxycoprostan-5β,6β-episulphide (XXII). In the hydrolysis of the mercapto-ol diacetates, the acetylthio groups are expected to be

[8] From the decomposition product of β-thiocyanato ethanol an urea compound having the same type of structure was isolated by Wagner-Jauregg. (T. Wagner-Jauregg and M. Härking, *Helv. Chim. Acta* **41**, 377 (1958).)

[9] E. E. van Tamelen, *J. Amer. Chem. Soc.* **73**, 3444 (1951).



more rapidly hydrolyzed.[2b] From these facts it may be assumed that in the formation of episulphide from the mercapto-ol diacetate, the leaving group requires a suitable bulkiness and electronegativity by the following mechanism.



Our previously reported experimental conditions for the lithium aluminum hydride reduction of 3β-hydroxycholestan-5α,6α-episulphide[2b] were used for the reduction of the cholestan-2,3-episulphides. In this case identical behavior such as formation of olefin and mercaptan was recognized. As separation of the reduction products through chromatography was unfortunately complicated with contamination of a disulphide (XXIV), the product was acetylated and then separated by direct crystallization or alumina chromatography. Results obtained in the reaction at the boiling point of the solvent used are summarized in Table 1. Free mercaptan was regenerated by further reduction of the acetylthio compound with lithium aluminum hydride. In the androstane series, the 2β,3β-episulphide was similarly reduced to 2β-mercaptan

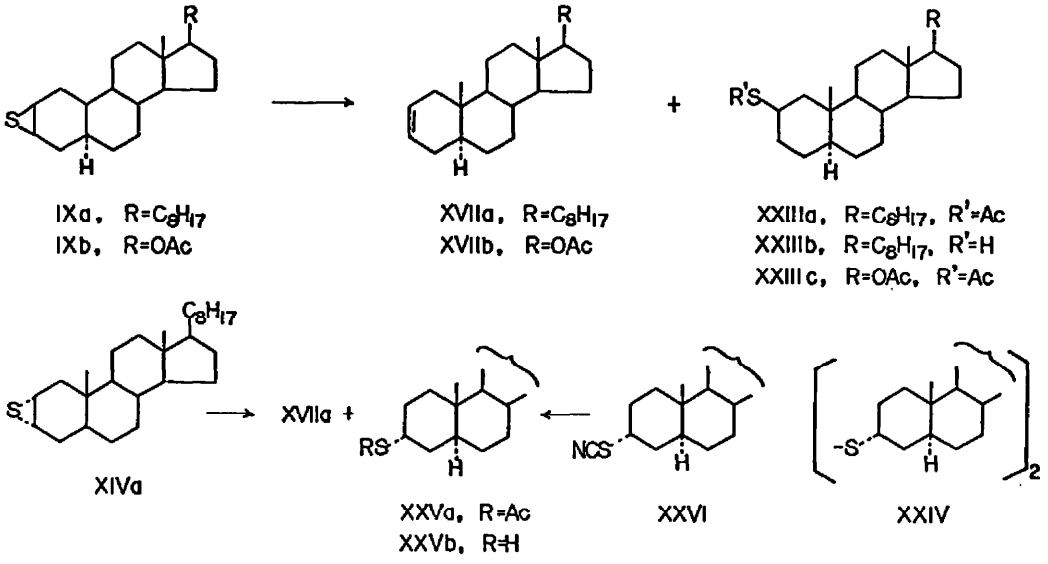


TABLE 1. YIELD (%) OF THE $LiAlH_4$ REDUCTION PRODUCT OF CHOLESTAN-2,3-EPISULPHIDES

Episulphide	Solvent	Recovered episulphides	Cholest-2-ene	Acetylthio-compound
2β,3β	ether:tetrahydrofuran (1:1)		16	60
2α,3α	ether:tetrahydrofuran (1:1)	62	17	
2α,3α	tetrahydrofuran		42	40

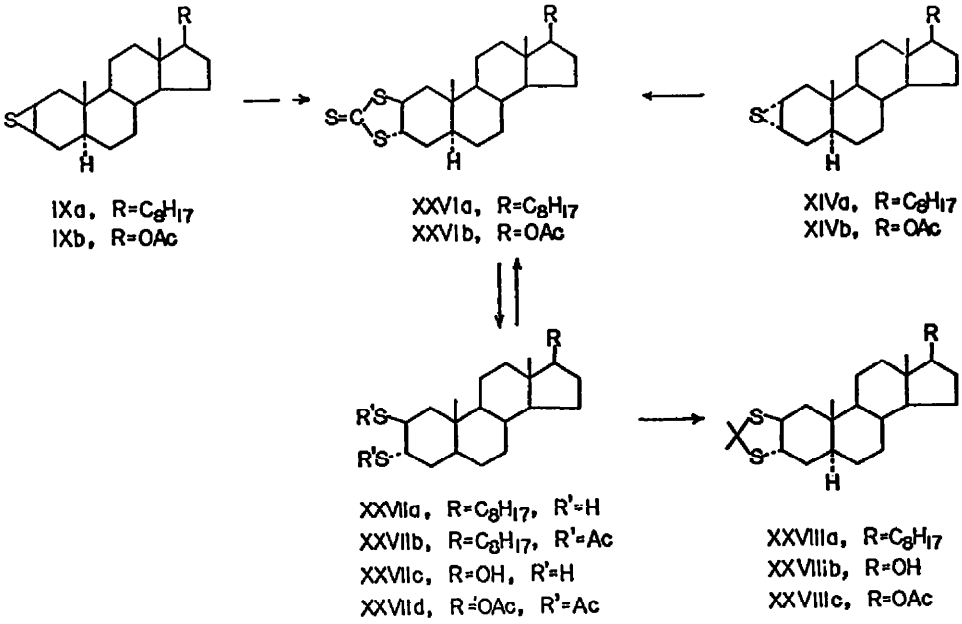
in an appropriate yield, but we could not isolate a 3α-mercaptan from the reduction product of 2α,3α-episulphide. These results agree qualitatively but differ quantitatively from those obtained by Lightner and Djerassi,[3a] and apparently are very dependent upon the reaction conditions. The fact that the reduction of the 2α,3α-episulphides required more drastic conditions is in accordance with the general rule that frontal attack of the aluminum hydride anion is more hindered. The result that the reduction product of 3α-thiocyanatocholestane (XXVI)[10,11] prepared from cholestanyl tosylate by Bourdon's[10] procedure gave the same mercaptan (XXVb), established the 3α-configuration of the ring opening compound of the 2α,3α-episulphide (XIV). The structure of 2β-mercaptocholestane (XXIIIb) was assumed from the NMR spectra (cf. Table 3). Acetylation contribution to the molecular rotation of 2β- and 3α-mercaptocholestane (XXIIIb and XXVb) is in full agreement with those of the corresponding cholestanols as shown in Table 2.

TABLE 2. MOLECULAR ROTATION (M_D) CONTRIBUTION OF ACYLATION

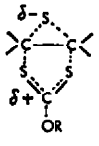
	M_D	ΔM_D(SAc-SH)		M_D	ΔM_D(OAc-OH)
2β,SH	+67		2β-OH	+147	
2β,SAc	+17	−50	2β-OAc	+116	−31
3α,SH	+126		3α-OH	+97	
3α,SAc	+171	+40	3α-OAc	+127	+32

[10] R. Bourdon, *Bull. Soc. Chim. Fr.* **1958**, 1117; *Ibid.* **1962**, 844.
[11] P. A. Bobbio and F. O. Bobbio, *Chem. Ber.* **95**, 2747 (1962).

In sugar chemistry, the reaction of episulphides with potassium alkyl xanthate is known to give yellow trithiocarbonates.[12] Similarly, heating of either 2α,3α- or 2β,3β-episulphides of both cholestane and androstane with the reagent for 24 to 30 hr afforded the same respective trithiocarbonate (XXVIa and XXVIb) as yellow crystals, in which *trans*-configuration, 2β,3α or 2α,3β, should be expected. Treatment of the



trithiocarbonate (XXVI) with lithium aluminum hydride, effectively used in the sugar series,[13] yielded a dimercaptan (XXVIIa and XXVIIc), which was readily condensed with acetone to give the isopropylidene derivative (XXVIIIa and XXVIIIb). During the lithium aluminum hydride reduction of the trithiocarbonate and acetonide formation of the resulting dimercaptan, the configuration was expected to be retained. This expectation was shown to be correct because the parent trithiocarbonate was regenerated from the dimercaptan by treatment of N,N'-thiocarbonylbis(2-methylimidazol). Nevertheless, in the trithiocarbonate formation the possibility of an intramolecular rearrangement through an intermediate, shown in the figure, as observed in a vicinal dihalide or halohydrin acetate[14] could not be excluded.



An attempt to clarify the configuration of the above compounds (XXVIa, XXVIIa

[12] A. M. Creighton and L. N. Owen, *J. Chem. Soc.* **1960**, 1024; D. L. Hall, L. Hough and R. A. Pritchard, *Ibid.* 1537 (1961) and cited Ref.

[13] S. M. Iqbal and L. N. Owen, *J. Chem. Soc.* 1032 (1960).

[14] G. H. Alt and D. H. R. Barton, *J. Chem. Soc.* 4284 (1954); D. H. R. Barton and W. J. Rosenfelder, *Ibid.* 1048 (1951); D. H. R. Barton and J. F. King, *Ibid.* 4398 (1958).

and XXVIIIa), by the addition reaction of dithiocyan with cholest-2-ene was fruitless, and the only information obtained was that from the NMR spectroscopy.

Recently, Kawazoe *et al.*[15] reported that the spatial vicinity of hydroxyl at 1,3-diaxial position to the angular methyl groups causes a remarkable downward shift of the methyl signal and that acetylation of that hydroxyl group causes a characteristic upward shift of the methyl signal. Such an acetylation effect was also found in the chemical shifts of 19-methyl groups of the compound having a 1,3-diaxial mercapto group, as shown in Table 3.[16] Moreover, in both the dimercaptan and its diacetate

TABLE 3. NMR DATA OF MERCAPTO-CHOLESTANES

	Chemical shift (τ)			($W_{H'}$, c.p.s.)		
	18-H	19-H	S—C—H (W_H)	O—C—H (W_H)	SAc	OAc
Cholestane	9·35	9·23				
-2β-SH	9·35	8·95	6.41 (15)			
-2β-SAc	9·35	9·10	5·95 (11)		7·71	
-3α-SH	9·35	9·22	6·48 (14)			
-3α-SAc	9·35	9·20	6·00 (10)		7·70	
3β-SH, 17β-OH	9·28	9·19	7·28 (22)			
3β-SAc, 17β-OAc	9·22	9·20	6·61 (25)		7·73	7·98
2α-SH, 3β-OH	9·36	9·14	7·29 (25)	6·79 (20)		
2α-SAc, 3β-OAc	9·35	9·06	6·28 (28)	5·31 (21)	7·71	8·00
2β-SH, 3α-OH	9·35	9·03	6·77 (13)	6·13 (9)		
2β-SAc, 3α-OAc	9·35	9·13	6·11 (19)	5·17 (6)	7·69	7·92
2β-OH, 3α-SH	9·35	9·00	6·76 (14)	6·03 (9)		
2β-OAc, 3α-SAc	9·35	9·08	6·13 (8)	5·05 (8)	7·68	7·95
2β,3α-di-SH	9·35	8·98	6·58 (13·5)			
2β,3α-di-SAc	9·36	9·09	6·06 (9)		7·68	

(XXVIIa and XXVIIb) the chemical shifts and the peak width at half height (W_H) of protons attached to the carbon bearing sulphur atom fell in the range characteristic of equatorial protons.[17] These data indicate that the dimercaptan (XXVII) should be *trans*-diaxial, 2β,3α, and that the trithiocarbonate (XXXIV) should also have 2β,3α-configuration. Ring formation in such a sterochemistry is only possible with ring A in the boat form, since two adjacent axial bonds in the chair-form are incapable of ring formation. It is of interest to note that the *trans*-diaxial mercapto-ol (IIIa or XIIIa) was also condensed successfully with acetone and N,N'-thiocarbonylbis-(2-methylimidazol) to yield the corresponding 2,2-dimethyl[1,3]oxathiolano derivative (XXIXa or XXXa), and the corresponding 2-thioxo[1,3]oxathiolano derivative (XXIXb or XXXb) respectively. In contrast, no acetonide formation was observed with the *trans*-diaxial-2β,3α-dihydroxy-5α,25D-spirostane[18,19] under the conditions used here.

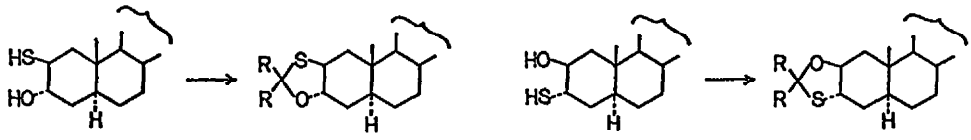
[15] K. Kawazoe, Y. Sato, M. Natzume, H. Hasegawa, T. Okamoto and K. Tsuda, *Chem. Pharm. Bull., Japan* **10**, 338 (1962).

[16] K. Tori and T. Komeno, *Tetrahedron*, **21**, 275 (1964).

[17] L. M. Jackman, *Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, pp. 115–119. Pergamon Press, London (1959).

[18] N. L. Wendler and H. L. Slates, *Chem. & Ind.* 167 (1955).

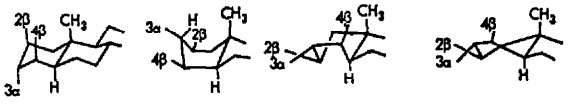
[19] Recently, acetonide formation of 2β,3α-diol in the series of triterpene has been reported. R. Teschesche, E. Henckel and G. Snatzke, *Tetrahedron Letters* 613 (1963).



IIIa XXIXa, R=Me XXIXb, R,R=S XIIIa XXXa, R=Me XXXb, R,R=S

Inspection of the Dreiding model shows that it is possible for A-ring in the steroid to have a boat conformation; two classical boat forms with C_2—C_5 or C_3—C_{10} at bowstern position and an intermediate of these two conformations, a skewed (or twist) boat form. It is assumed that in such a situation the skewed form[20] is preferred because the dihedral angle of 2β-C_2—C_3-3α and the distance between 2β- and 3α-substituent are minimum and the fusion of a five-membered ring to A-ring is more favorable. This assumption was established from the NMR signal pattern of C_2 and C_3 protons, which will be reported in detail elsewhere.

As mentioned above both 2β,3β- and 2α,3α-episulphide reacted with potassium methylxanthate to give 2β,3α-trithiocarbonate, and *trans*-diaxial 2β-mercapto-3α-ol or 3α-mercapto-2β-ol condensed with acetone or N,N'-thiocarbonylbis(2-methylimidazol) to yield the [1,3]oxathiolano derivative. The formation of such a five-membered ring at positions 3α and 4β is only possible when ring A is in the boat form B in comparison to the other three possible forms, but is the least favorable because of interaction between the 19-methyl group and 3β-proton.



(A) (B) (C) (D)

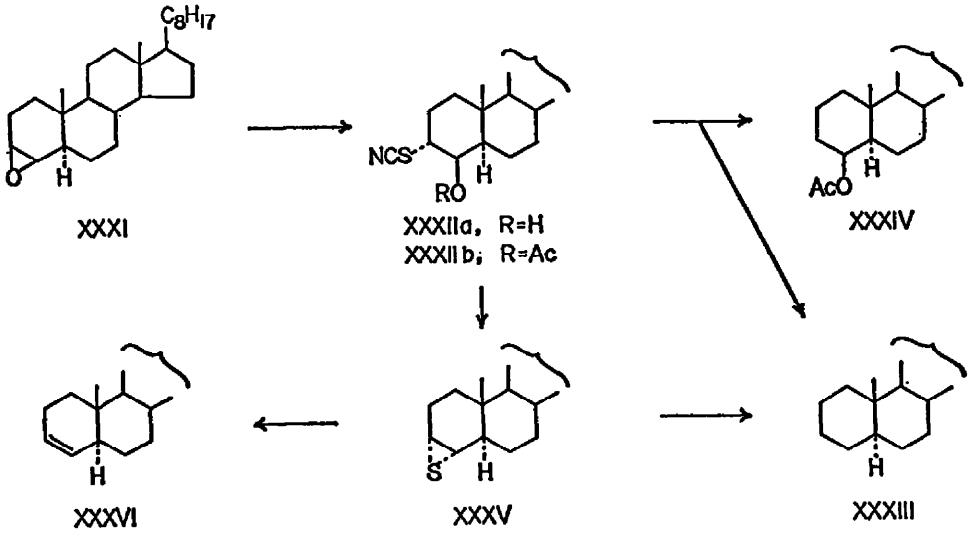
When 5α-cholestan-3β,4β-oxide (XXXI), prepared by the Fürst method,[21] was treated with thiocyanic acid, there was obtained 3α-thiocyanato-5α-cholestan-4β-ol (XXXIIa), which was easily acetylated to 4-acetate (XXXIIb). Chemical evidence of 4β-configuration of the newly formed hydroxyl group was obtained from the result that Raney nickel desulfurization of XXXIIb provided 63% of 5α-cholestane (XXXIII) and 13% of 4β-acetoxy-5α-cholestane (XXXIV). Hydrolysis of the acetate (XXXIIb) with potassium hydroxide and absolute ethanol afforded 3α,4α-episulphide (XXXV). In the NMR spectrum the observed coupling constants between the 3β- or 4β-proton and the adjacent methylene or methyne protons have very reasonable values for the assigned structure. The structure was further confirmed by Raney nickel or zinc–acetic acid reduction and there was obtained 5α-cholestane (XXXIII) and 5α-cholest-3-ene (XXXVI), respectively. The ORD curve of cholestan-3α,4α-episulphide (XXXV) showed a positive Cotton effect and the result cited in the earlier experiment[22,23] should be corrected.

[20] J. B. Hendrickson, *J. Amer. Chem. Soc.* **83**, 4537 (1961). According to Hendrickson, this dihedral angle was calculated to be 49·3°, and in cyclohexane the skewed form was more stable by 1·6 kcal/mole than the boat form.

[21] A. Fürst and R. Scotoni, Jr., *Helv. Chim. Acta* **36**, 1332 (1953).

[22] C. Djerassi, H. Wolf, D. A. Ligtner, E. Bunnenberg, K. Takeda, T. Komeno and K. Kuriyama, *Tetrahedron* **19**, 1547 (1963).

[23] cf. D. A. Lightner and C. Djerassi, *Tetrahedron*, in press.



Ring opening of 5α-cholestan-3α,4α-oxide (XXXVIIa) and 17β-acetoxy-5α-androstan-3α,4α-oxide (XXXVIIb) by thiocyanic acid afforded the expected 4β-thiocyanato-3α-ol (XXXVIIIa and XXXVIIIc), respectively. Hydrolysis of (XXXVIIIc) with potassium carbonate and methanol did not give the episulphide but the parent oxide (XXXVIIb). The expected 3β,4β-episulphide (XXXIXa or XXXIXb) was obtained by alkaline treatment of the acetate (XXXVIIIb) or the mesylate (XXXVIIId). Lithium aluminum hydride reduction of (XXXVIIIa) afforded 4β-mercapto-3α-ol (XLa), which could not be condensed with acetone or N,N′-thiocarbonylbis(2-methylimidazol) to give the [1,3]oxathiolano derivative.

Kiliani and Jones oxidation of 4β-thiocyanato-3α-ol (XXXVIIIa) gave a mixture of 4β-thiocyanato-3-one (XLI) and 4α-thiocyanato-3-one (XLII), which were separated by fractional crystallization. Attempts to separate the mixture by alumina chromatography led to isolation of the oxothiazoline compound (XLII), in which the IR spectrum showed a lactam band at 3145, 3030 and 1680 cm^{-1}. Prolonged oxidation of (XXXVIIIa) gave only 4α-thiocyanato-3-one (XLII). It is of interest to note that the Cotton effect of the thiocyanato-ketone is predictable by the axial haloketone rule, thus the 4β-thiocyanato-3-one exhibited a positive Cotton curve, while the 4α-thiocyanato-3-one showed a negative curve.

Lithium aluminum hydride reduction of 4α-thiocyanato-3-one (XLII) afforded a mixture of 4α-thiocyanato-3α-ol (XLV) and 4α-thiocyanato-3β-ol (XLVI), which was separated by means of Florisil chromatography. From the NMR data as shown in Table 4, the less polar product was assigned as 4α-mercapto-3α-ol and the other as 4α-mercapto-3β-ol.

Both *trans*-diequatorial and *cis*-mercapto-ol obtained could be condensed with acetone or N,N′-thiocarbonylbis(2-methylimidazol), to yield the [1,3]oxathiolano compound (XLVIa, XLVIb, XLVIIa or XLVIIb), respectively, but the 3α,4β-diaxial compound (XLa) could not be formed from such five-membered ring derivatives.

The expected trithiocarbonate also could not be isolated from the reaction product of both 3α,4α- and 3β,4β-episulphide with potassium methylxanthate. This result

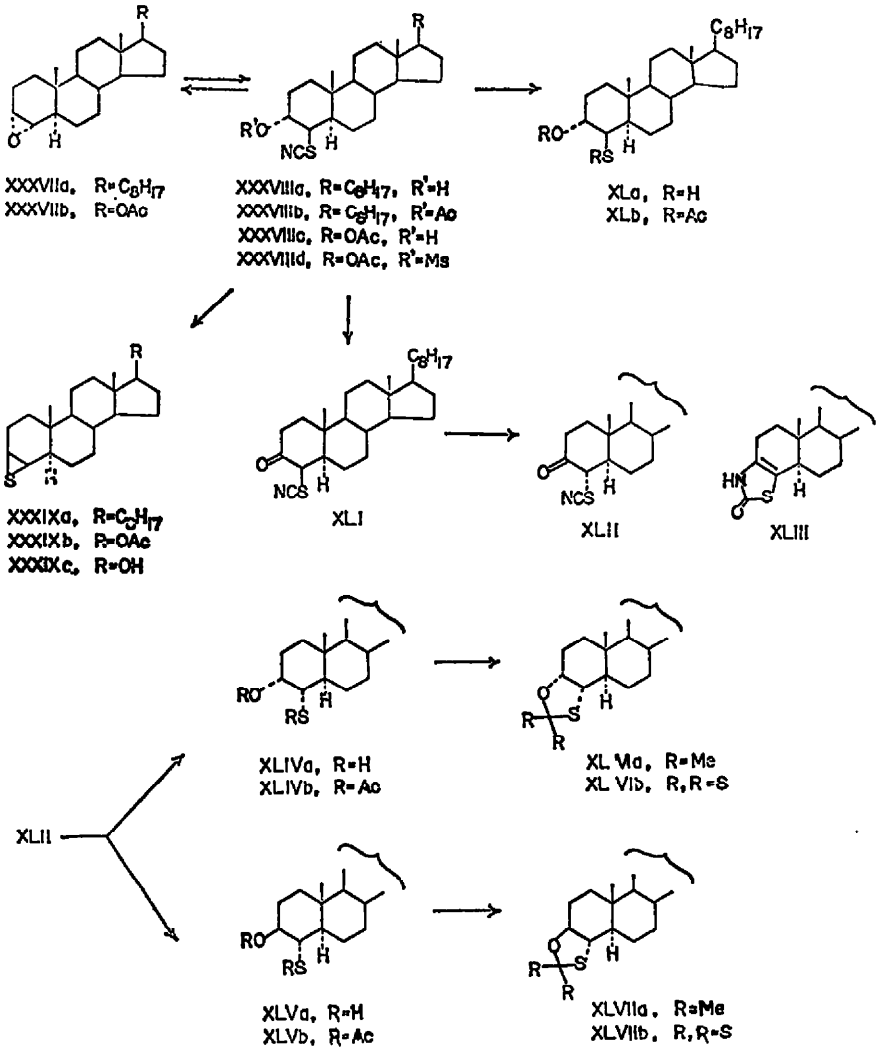


TABLE 4. NMR DATA OF VICINAL 3,4-SUBSTITUTED MERCAPTO-OL

	Chemical shift (τ)						Coupling constant (J, c.p.s.)		
	18-H	19-H	3-H	4-H	OAc	SAc	J_{3H-3H}	J_{3H-4H}	J_{4H-5H}
3α-OH 4β-SH	9·35	9·03	6·02	6·91			$W_H(3H) = 7·0$		$W_H(4H) = 11·0$
Diacetate	9·35	9·15	5·17	6·27	7·93	7·70	$W_H(3H) = 7·5$		$W_H(4H) = 8·0$
3α-OH 4α-SH	9·35	9·17	6·22	6·95			2·5 2·5	2·5	10·6
Diacetate	9·35	9·07	4·95	6·24	7·95	7·73	2·5 2·5	2·5	12·0
3β-OH 4α-SH	9·35	9·16	6·82	7·45			10·0 4·7	10·0	10·0
Diacetate	9·35	9·07	5·31	6·38	8·03	7·70	11·0 5·3	11·0	11·0

suggests that a transition state for the reaction, with favorable conformation or required proximity between the 3α- and 4β-substituents, is unlikely.*

EXPERIMENTAL

All m.ps were determined on a Kofler block and are uncorrected. Optical rotations were measured in $CHCl_3$ unless mentioned otherwise, using a Rudolf Photoelectronic Polarimeter, model 200, and ORD curves were taken with a Rudolf automatic recording spectropolarimeter. The UV absorption spectra were measured with a Hitachi Recording UV spectrophotometer, EPs-2, and the IR spectra were taken with a Koken IR spectrophotometer, Model DS-301. The NMR spectra were run in deuteriochloroform solution with a Varian A-60 spectrometer, tetramethylsilane serving as internal standard.

2β-Thiocyanato-5α-cholestan-3α-ol (IIa)

To a mixture of KCNS (20 g) dissolved in a small volume iced water and ether (40 ml), phosphoric acid (30 g) was added in small portions and shaken to move formed free thiocyanic acid to ether. The pink-colored thiocyanic acid solution was dried (Na_2SO_4) and added to a solution of Ia[24] (3·50 g) in ether (10 ml). The reaction mixture was allowed to stand overnight at room temp. The solution was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated to dryness. The residue was twice recrystallized from hexane to yield IIa, (3·20 g) as needles, m.p. 161–163°, $[\alpha]_D^{21}$ +27·9° (c = 1·112), ν_{max}^{Nujol} 3553, 2161, 1035, 1015 cm^{-1}. (Found: C, 75·76; H, 10·68; N, 3·20; S, 7·12. $C_{28}H_{47}NOS$ requires: C, 75·44; H, 10·63; N, 3·14; S, 7·19%). This compound was acetylated with pyridine and acetic anhydride. The product was recrystallized from ethanol to give an acetate (IIb), m.p. 125–127°, $[\alpha]_D^{21}$ +58·2° (c = 1·101), ν_{max}^{Nujol} 2164, 1748, 1242, 1229 cm^{-1}. (Found: C, 73·99; H, 10·12; N, 2·93; S, 6·60. $C_{30}H_{49}NO_2S$ requires: C, 73·87; H, 10·13; N, 2·87; S, 6·57%).

2β-Mercapto-5α-cholestan-3α-ol (IIIa)

To a stirred suspension of $LiAlH_4$ (117 mg) in ether (10 ml), a solution of IIa (686 mg) in ether (40 ml) was added dropwise for a period of 30 min at room temp, and stirred under reflux for additional 1 hr. After cooling, the reaction mixture was poured into iced 5% HCl, and extracted with ether. The ethereal solution was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The resulting residue (655 mg) was chromatographed over Florisil (20 g). Elution with pet. ether–benzene (95:5–1:1) afforded the material, which was recrystallized from acetone to give IIIa (455 mg) as needles, m.p. 122–124°, $[\alpha]_D^{16}$ +30·1° (c = 0·894), ν_{max}^{Nujol} 3416, 1036, 1013 cm^{-1}. (Found: C, 77·17; H, 11·51; S, 7·31. $C_{27}H_{48}OS$ requires: C, 77·08; H, 11·50; S, 7·62%). This compound was acetylated with pyridine and acetic anhydride and the product was recrystallized from ethanol to yield IIIb as small needles, m.p. 119–120°, $[\alpha]_D^{17}$ +34·2° (c = 0·933), λ_{max}^{alc} 231 mμ (ϵ 4670), ν_{max}^{Nujol} 1746, 1693, 1240, 1116 cm^{-1}. (Found: C, 75·86; H, 10·24; N, 3·43; S, 7·55. $C_{29}H_{48}NOS$ requires: C, 75·79; H, 10·22; N, 3·16; S, 7·23%).

2-Substituted [1,3]*oxathiolano compound of the mercapto-ol* (IIIa)

(a) *2,2-Dimethyl compound* (XXIXa). A solution of IIIa (548 mg) and *p*-toluenesulphonic acid (75 mg) in acetone (40 ml) was refluxed for 5 hr, poured into iced Na_2CO_3 solution, and extracted with ether. The product was dissolved in pet. ether and passed through a column of Al_2O_3 (11 g). The eluted material was recrystallized from acetone to yield XXIXa (477 mg) as needles, m.p. 141·5–143°, $[\alpha]_D^{25}$ +81·8° (c = 1·038), ν_{max}^{Nujol} 1367 cm^{-1}. (Found: C, 78·02; H, 11·24; S, 6·98. $C_{30}H_{52}OS$ requires: C, 78·19; H, 11·38; S, 6·96%).

(b) *2-Thioxo compound* (XXIXb). A solution of IIIa (270 mg) and N,N′-thiocarbonylbis(2-methylimidazol) (162 mg) in chloroform (20 ml) was refluxed for 5·5 hr. After cooling, the chloroform solution was washed successively with HCl, Na_2CO_3 solution, and water, dried (Na_2SO_4), and

* Similarly attempted conversions of 3β-hydroxycholestan-5α,6α-, 5β,6β-episulphide and 3,3-ethylenedioxypregn-5-en-16β,17β-episulphide to the corresponding trithiocarbonates were all unsuccessful.

[24] A. Fürst and P. A. Plattner, *Helv. Chim. Acta* **32**, 275 (1949).

evaporated. The residue was chromatographed over Al_2O_3 (5·5 g) and the material (96 mg) eluted with pet. ether–benzene (9:1) was recrystallized from ether–ethanol to give XXIXb (68 mg) as colorless plates, m.p. 152–154·5°, λ_{max}^{alc} 282 mμ (ε 17,380), 370 mμ (ε 100), $\nu_{max}^{CCl_4}$ 1200 cm^{-1}. (Found: C, 72·96; H, 10·06; S, 13·63. $C_{28}H_{46}OS_2$ requires: C, 72·67; H, 10·02; S, 13·81%).

Cholestan-2β,3β-episulphide (IXa)

(a) *From the thiocyanatohydrin* (IIa). A mixture of IIa (600 mg) in 5% KOH–methanol (20 ml) was refluxed for 10 min and poured into water. The precipitates were collected by filtration, dried, and recrystallized from acetone to yield IXa (468 mg), m.p. 120–122°, $[\alpha]_D^{24}$ +40·6° (*c* – 1·053), λ_{max}^{alc} 207 mμ (ε 2130), 262 mμ (ε 48). (Found: C, 80·52; H, 11·51; S, 7·96. Calc. for $C_{27}H_{46}S$: C, 80·73; H, 11·55; S, 7·89%). Reported[3a] m.p. 113–115°, $[\alpha]_D^{27}$ +43°.

(b) *From the mercapto-ol diacetate* (IIIb). A mixture of IIIb (83 mg) in 5% KOH–methanol (5 ml) was refluxed for 10 min. After working up as above described, IXa (65 mg), m.p. 120–122°, was obtained.

Alkaline treatment of the mercapto-ol (IIIa)

A solution of IIIa (530 mg) in ether (5 ml) was added to 5% KOH aq–methanol (20 ml) and refluxed for 30 min. To the mixture, water was added and extracted with chloroform. The product (510 mg) was dissolved in pet. ether and chromatographed over Florisil (20 g). Elution with pet. ether–benzene (1:1) afforded IIIa (412 mg), m.p. 121–123°. Further elution with benzene–chloroform (1:1) gave the material, which was recrystallized from chloroform–methanol to yield X (95 mg), m.p. 209–212° (dec), $[\alpha]_D^{25}$ −71·9° (*c* – 1·170, pyridine), ν_{max}^{Nujol} 3504, 1006 cm^{-1}. (Found: C, 77·31; H, 11·26; S, 7·65. $C_{54}H_{94}O_2S$ requires: C, 77·26; H, 11·29; S, 7·64%. Rast 874·4, Calc. M.W. 839·4).

2α-*Thiocyanato-5α-cholestan-3-one* (IVa)

(a) *From the thiocyanatohydrin* (IIa). To a solution of IIa (500 mg) in purified acetone (20 ml), 2-equivalents of Jones' reagent[25] were added. The reaction mixture was stirred for 10 min at room temp, poured into water, and extracted with ether. The ethereal solution was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The residue was three times recrystallized from aqueous acetone to yield IVa (258 mg) as needles, m.p. 150–152°, $[\alpha]_D^{19}$ −74·4° (*c* – 1·001), ν_{max}^{Nujol} 2156, 1709 cm^{-1}. ORD: (*c* = 0·203, methanol), $[\alpha]_{700}$ −12°, $[\alpha]_{500}$ −12°, $[\alpha]_{309}$ +284° (peak), $[\alpha]_{295}$ +128°. NMR: (18-H) 9·32τ; (19-H) 8·88; (2β-H) 5·64; (1β-H) 7·28; $J_{2\beta-H:1\beta-H}$ = 6·4 c/s; $J_{2\beta-H:1\alpha-H}$ = 13·0; $J_{1\alpha-H:1\beta-H}$ = −12·5. (Found: C, 75.86; H, 10·24; N, 3·43; S, 7·55. $C_{28}H_{45}NOS$ requires: C, 75·79; H, 10·22; N, 3·16; S, 7·23%).

(b) *From the bromoketone* (V). To a solution of V (900 mg) in acetone (30 ml), KCNS (600 mg) was added. The resulting mixture was stirred for 8 hr at room temp, poured into water, and extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and the solvent was evaporated. The residue was three time recrystallized from aqueous acetone to give IVa (685 mg), m.p. 150–152°, which was identical with the ketone prepared in (a) by mixed m.p. and comparison of the IR spectra.

(c) *Conversion to 5α-cholestan-3-one.* A suspension of IVa (200 mg) and Zn dust (2 g) in acetic acid (15 ml) was stirred under reflux for 3 hr, then poured into water, and extracted with ether. The extract was washed successively with water, Na_2CO_3 solution, and water, dried (Na_2SO_4), and evaporated. The residue (173 mg) was chromatographed over Al_2O_3 (6 g). The material eluted with pet. ether–benzene (1:1) was recrystallized from ethanol to yield 5α-cholestan-3-one (152 mg), m.p. 129–131°. This compound was identical with the authentic sample by mixed m.p. and comparison of the IR spectra.

2′-*Oxothiazolo*[5′,4′-2,3]-*5α-cholest*-2-*ene* (VIII)

A solution of IVa (469 mg) in a mixture of dioxane (5 ml), acetone (4 ml), and 36% HCl (2 ml) was warmed on a steam-bath for 2 hr. In the brown colored reaction mixture, the appeared crystals were collected by filtration and recrystallized from chloroform–methanol to yield VIII (246 mg), m.p.

[25] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

325–327° (dec), λ_{max}^{alc} 251 mμ (ε 5250), ν_{max}^{Nujol} 3146, 3030, 1680, 1574 cm^{-1}. (Found: C, 75·53; H, 10·18; N, 3·13; S, 7·37. $C_{28}H_{45}NOS$ requires: C, 75·79; H, 10·22; N, 3·16; S, 7·23%).

2α-Mercapto-5α-cholestan-3β-ol (VIa)

(a) *From 3-oxo-5α-cholestan-2α-ethylxanthate* (IVb). Compound IVb was prepared according to Djerassi *et al.*[6] Physical constants of the compound obtained by us are as follows, m.p. 115–116°, $[\alpha]_D^{21}$ −75·2° (*c* = 0·922), λ_{max}^{alc} 207·5 mμ (ε 7580), 223 mμ (ε 7420), 279·5 mμ (ε 10,440), 355 mμ (ε 70), ν_{max}^{Nujol} 1712 cm^{-1}. NMR: (18-H) 9·32τ: (19-H) 8·82; (2β-H) 5·29; (1β-H) 7·47; $J_{2\beta-H:1\beta-H}$ = 6·0 c/s; $J_{2\beta-H:1\alpha-H}$ = 13·0; $J_{1\alpha-H:1\beta-H}$ = −12·5. (Found: C, 71·34; H, 10·02; S, 12·40. Calc. for $C_{30}H_{50}O_2S_2$: C, 71·09; H, 9·94; S, 12·65%). Reported[6] m.p. 116·5–118°, $[\alpha]_D^{25}$ −64·5°. A solution of this xanthate (1·50 g) in ether (50 ml) was added to a stirred suspension of $LiAlH_4$ (450 mg) in ether (10 ml), refluxed for 3 hr, and then poured into iced dil. HCl. The ethereal solution was washed with Na_2CO_3 solution and water, and evaporated. The residue was twice recrystallized from acetone to yield VIa (1·20 g), m.p. 125–127°, $[\alpha]_D^{19}$ +10·9° (*c* = 0·943), λ_{max}^{alc} 205 mμ (ε 670), ν_{max}^{Nujol} 3360, 2575 cm^{-1}. (Found: C, 76·83; H, 11·48; S, 7·25. $C_{27}H_{48}OS$ requires: C, 77·08; H, 11·50; S, 7·62%). Reported[6] m.p. 122–124°, $[\alpha]_D^{25}$ +10·6°. This compound was acetylated with pyridine and acetic anhydride and recrystallized from ethanol to give VIb, m.p. 108–110°, $[\alpha]_D^{18}$ −46·7° (*c* = 0·982), λ_{max}^{alc} 232·5 mμ (ε 4480), ν_{max}^{Nujol} 1743, 1700, 1233, 1114 cm^{-1}. (Found: C, 73·96; H, 10·47; S, 6·44. Calc. for $C_{31}H_{52}O_2S$: C, 73·96; H, 10·30; S, 6·30%).

(b) *From the thiocyanatoketone* (IVa). The IVa (440 mg) was reduced with $LiAlH_4$ (120 mg) to give VIa (260 mg), m.p. 125–127°, which was identical with the compound prepared from IVb by mixed m.p. and comparison of the IR spectra.

2-Substituted [1,3] *oxathiolano compound of the 2α-mercapto-3β-ol* (VIa)

(a) 2,2-*Dimethyl compound* (VIIa). A solution VIa (360 mg) and *p*-toluenesulphonic acid (30 mg) in acetone (15 ml) was refluxed for 5 hr, poured into iced Na_2CO_3 solution, and extracted with ether. The extract was dissolved in pet. ether and chromatographed over Al_2O_3 (9 g). The material eluted with pet. ether was recrystallized from ether–acetone to give VIIa (320 mg), m.p. 120–121°, $[\alpha]_D^{28}$ +45·2° (*c* = 0·991), $\nu_{max}^{CHCl_3}$ 1366 cm^{-1}. (Found: C, 78·27; H, 11·48; S, 7·12. $C_{30}H_{52}OS$ requires: C, 78·19; H, 11·38; S, 6·96%).

(b) 2-*Benzylidene compound* (VIIb). A solution of VIa (1·022 g), *p*-toluenesulphonic acid (50 mg), and benzaldehyde (1·0 g) in benzene (100 ml) was refluxed for 5 hr. The product (1·242 g) was chromatographed over Al_2O_3 (20 g). The material (621 mg) eluted with pet. ether–benzene (9:1) was recrystallized from ether–acetone to yield VIIb (430 mg), m.p. 155–157°, $[\alpha]_D^{22\cdot5}$ +116·1° (*c* = 1·059), ν_{max}^{Nujol} 1048, 1026, 701 cm^{-1}. (Found: C, 80·52; H, 10·43; S, 6·40. $C_{34}H_{52}OS$ requires: C, 80·25; H, 10·30; S, 6·30%).

(c) 2-*Thioxo compound* (VIIc). A solution of VIa (50 mg) and N,N′-thiocarbonylbis(2-methylimidazol) (32 mg) in chloroform (4 ml) was refluxed for 3·5 hr. The product was chromatographed over Al_2O_3 (1·5 g) and the material eluted with pet. ether–benzene (9:1) was recrystallized from acetone to give VIIc (22 mg) as colorless plates, m.p. 125–126·5°, $[\alpha]_D^{22\cdot5}$ −133·2° (*c* = 1·0746) $\nu_{max}^{CCl_4}$ 1721 (ω), 1200 cm^{-1}. (Found: C, 72·12; H, 10·30; S, 12·96. $C_{28}H_{46}OS_2 \cdot \frac{1}{2} C_3H_6O$ requires: C, 72·04; H, 10·04; S, 13·04%).

3α-Thiocyanato-5α-cholestan-2β-ol (XIIa)

Compound XIa, m.p. 89–90°, $[\alpha]_D^{21}$ +58·5° (*c* = 1·011) (reported m.p. 87·5–88·5°, $[\alpha]_D$ +50·5°) was used as the starting material. This oxide (610 mg) was treated with thiocyanic acid in ether as described above and the product was recrystallized from acetone–hexane and further from acetone–methanol to yield XIIa (596 mg), as colorless needles, m.p. 165–167°, $[\alpha]_D^{22}$ +43·0° (*c* = 1·060), ν_{max}^{Nujol} 3538, 2172 cm^{-1}. (Found: C, 75·60; H, 10·61; N, 3·07; S, 6·95. $C_{28}H_{47}NOS$ requires: C, 75·44; H, 10·63; N, 3·14; S, 7·19%). This compound was acetylated with pyridine and acetic anhydride to give XIIb, which was recrystallized from ethanol to needles, m.p. 111–113°, $[\alpha]_D^{23}$ +59·2° (*c* = 1·040), ν_{max}^{Nujol} 2171, 1743, 1235 cm^{-1}. (Found: C, 73·86; H, 10·35; N, 3·02; S, 6·63. $C_{30}H_{49}NO_2S$ requires: C, 73·87; H, 10·13; N, 2·87; S, 6·57%).

3α-Mercapto-5α-cholestan-2β-ol (XIIIa)

A solution of XIIa (1·009 g) in ether (60 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (172 mg) in ether (20 ml), refluxed for 1 hr, and then poured into iced 5% HCl. The ethereal solution was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and the solvents was evaporated. The residue (0·953 g) was purified by chromatography over Florisil (30 g). The material eluted with pet. ether and benzene (2:1) was recrystallized from methanol to yield XIIIa (710 mg) as colorless leaflets, m.p. 118–120°, $[\alpha]_D^{30}$ +53·2° (c = 1·055), ν_{max}^{Nujol} 3350, 2562 cm^{-1}. (Found: C, 76·92; H, 11·62; S, 7·55. $C_{27}H_{48}OS$ requires: C, 77·08; H, 11·50; S, 7·62%). This compound was acetylated with pyridine and acetic anhydride to give XIIIb, which was recrystallized from ethanol to needles, m.p. 141–143°, $[\alpha]_D^{22}$ +38·9° (c = 1·017), λ_{max}^{alc} 231 mμ (ε 4870), ν_{max}^{Nujol} 1744, 1703, 1236, 1105 cm^{-1}. (Found: C, 73·79; H, 10·33; S, 6·15. $C_{31}H_{52}O_2S$ requires: C, 73·96; H, 10·30; S, 6·30%).

2-Substituted [1,3]*oxathiolano compound of the mercapto-ol* (XIIIa)

(a) *2,2-Dimethyl compound* (XXXa). A solution of XIIIa (499 mg) and *p*-toluenesulphonic acid (70 mg) in acetone (30 ml) was refluxed for 6 hr, poured into iced Na_2CO_3 solution, and extracted with ether. The product was chromatographed over Florisil (10·5 g). The material (305 mg) eluted with pet. ether was recrystallized from acetone to give XXXa as needles, m.p. 152–153°, $[\alpha]_D^{24\cdot5}$ +90·3° (c = 0·691), ν_{max}^{Nujol} 1367 cm^{-1}. (Found: C, 78·35; H, 11·38; S, 7·05. $C_{30}H_{52}OS$ requires: C, 78·19; H, 11·38; S, 6·96%). Elution with benzene afforded the recovered XIIIa (80 mg), m.p. 117–119°.

(b) *2-Thioxo compound* (XXXb). A solution of XIIIa (59 mg) and N,N′-thiocarbonylbis(2-methylimidazol) (36 mg) in chloroform (5 ml) was refluxed for 5·5 hr. The product was dissolved in pet. ether and chromatographed over Al_2O_3 (2·0 g). The material eluted with pet. ether was recrystallized from acetone to yield XXXb (17 mg) as needles, m.p. 177–179°, λ_{max}^{alc} 282 mμ (ε 17380), 370 mμ (ε 100), $\nu_{max}^{CCl_4}$ 1200 cm^{-1}. (Found: C, 72·53; H, 10·09. $C_{28}H_{46}OS_2$ requires: C, 72·67; H, 10·02%).

5α-Cholestan-2α,3α-episulphide (XIVa)

(a) *From the thiocyanatohydrin* (XIIa). A mixture of XIIa (1·700 g) in 4% KOH–methanol (40 ml) was refluxed for 10 min, poured into water, and extracted with ether. The product (1·528 g) was purified by chromatography over Al_2O_3 (45 g). The material eluted with pet. ether was recrystallized from acetone to give XIVa (1·252 g) as colorless needles, m.p. 123–124°, $[\alpha]_D^{23}$ +26·2° (c = 0·988), λ_{max}^{alc} 262 mμ (ε 48). (Found: C, 80·85; H, 11·46; S, 7·71. $C_{27}H_{46}S$ requires: C, 80·52; H, 11·51; S, 7·96%).

(b) *From the mercapto-ol diacetate* (XIIIb). To a solution of XIIIb (409 mg) in ethanol (20 ml), KOH (800 mg) was added. The resulting mixture was refluxed for 20 min, poured into water, and extracted with ether. The product was dissolved in pet. ether and passed through a column of Al_2O_3 to yield XIVa (315 mg), m.p. 122–123°.

Alkaline treatment of the mercapto-ol (XIIIa)

A solution of XIIIa (346 mg) in ether (5 ml) was added to 5% KOH–methanol (19 ml) and refluxed for 30 min. The reaction mixture was poured into water, and extracted with chloroform. The product was dissolved in benzene and chromatographed over Al_2O_3 (10 g). The material eluted with benzene–ether (1:1) was recrystallized from methylene chloride–acetone to give XV (253 mg), m.p. 205–206°, $[\alpha]_D^{25}$ −23·5° (c = 1·128), ν_{max}^{Nujol} 3400 cm^{-1}. (Found: C, 77·04; H, 11·48; S, 7·30. $C_{54}H_{94}O_2S_2$ requires: C, 77·26; H, 11·29; S, 7·64%. Rast 863·9, Calc. M.W. 839·4). When this disulphide (153 mg) was reduced with $LiAlH_4$ (30 mg) in ether (20 ml), followed by acetylation, XIIIb was obtained, (152 mg), m.p. 140–142°.

Cholestane-2β,3α-dithiol trithiocarbonate (XXVIa)

(a) *From the 2β,3β-episulphide* (IXa). To a solution of KOH (7 g) in methanol (50 ml), CS_2 (17 ml) and IXa (2·070 g) were added. The resulting mixture was refluxed for 24 hr and poured into water. The appeared precipitates were collected by filtration, dried, dissolved in pet. ether, and chromatographed over Al_2O_3 (60 g). The material (1·940 g) eluted with pet. ether–benzene (19:1–9:1) was recrystallized from ether–ethanol to give XXVIa (1·318 g) as yellow leaflets, m.p. 132–133°, $[\alpha]_D^{24}$ +61·7° (c = 0·893), λ_{max}^{alc} 242 mμ (ε 1050), 317 mμ (ε 13490), 450 mμ (ε 96), ν_{max}^{Nujol} 1108, 1062, 860 cm^{-1}. (Found: C, 70·30; H, 9·77; S, 20·19. $C_{28}H_{46}S_3$ requires: C, 70·23; H, 9·68; S, 20·09%).

(b) *From the* 2α,3α-*episulphide* (XIVa). To a solution of KOH (4 g) in methanol (30 ml), XIVa (949 mg) and CS_2 (10 ml) was added and refluxed for 30 hr. After working up as described above, there was obtained the trithiocarbonate (683 mg), m.p. 132–133°, which was identical with the compound prepared in (a) by mixed m.p. and comparison of the IR spectra.

(c) *From the* 2β,3α-*dithiol* (XXVIIa). A solution of XXVIIa (51 mg) and N,N′-thiocarbonylbis(2-methylimidazol) (32 mg) in chloroform (4 ml) was refluxed for 5·5 hr. The solution was washed successively with HCl, Na_2CO_3 solution, and water, dried (Na_2SO_4), and evaporated. The product was chromatographed over Al_2O_3 (2 g). Elution with pet. ether afforded XXVIa (14 mg), m.p. 129–131°.

5α-*Cholestane*-2β,3α-*dithiol* (XXVIIa)

To a stirred suspension of $LiAlH_4$ (580 mg) in ether (30 ml), a solution of XXVIa (1·216 g) in ether (70 ml) was added dropwise over 15 min. The reaction mixture was further stirred under reflux for 2 hr and poured into iced 5% HCl. The ethereal solution was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The residual solid (1·103 g) was twice recrystallized from acetone to XXVIIa (716 mg) as colorless leaflets, m.p. 115–116°, $[\alpha]_D^{28}$ +41·7° (c = 1·006). (Found: C, 74·46; H, 11·32; S, 14·77. $C_{27}H_{48}S_2$ requires: C, 74·24; H, 11·08; S, 14·68%). This compound was acetylated with pyridine and acetic anhydride to yield XXVIIb, which was recrystallized from aqueous acetone to colorless needles, m.p. 127–129°, $[\alpha]_D^{28}$ −12·1° (c = 1·030), λ_{max}^{alc} 232 mμ (ε 8820), ν_{max}^{Nujol} 1695, 1136, 1121, 955 cm^{-1}. (Found: C, 71·64; H, 10·29; S, 12·58. $C_{31}H_{52}O_2S_2$ requires: C, 71·48; H, 10·06; S, 12·31%). A solution of XXVIIa (310 mg) and *p*-toluenesulphonic acid (30 mg) in acetone (12 ml) was refluxed for 5 hr, poured into iced Na_2CO_3 solution, and extracted with ether. The product was recrystallized from acetone to give XXVIIIa (289 mg), m.p. 122–123°, $[\alpha]_D^{28}$ + 69·9° (c = 0·999), $\nu_{max}^{CHCl_3}$ 1365 cm^{-1}. (Found: C, 75·74; H, 11·22; S, 13·23. $C_{30}H_{52}S_2$ requires: C, 75·56; H, 10·99; S, 13·45%).

2β-*Thiocyanato*-5α-*androstane*-3α,17β-*diol* 17-*acetate* (IIc)

Compound Ib (3.995 g, m.p. 108–110°, $[\alpha]_D^{20}$ +20·3° (c = 1·065); reported[26] m.p. 110–111°, $[\alpha]_D^{20}$ +20·6°) was added to the thiocyanic acid solution prepared from KSCN (30 g), H_3PO_4 (70 g), and ether (50 ml) and allowed to stand overnight at room temp. The ethereal solution was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated to dryness. The residue was recrystallized from methanol to give IIc as colorless needles (3·295 g, 70·1%), m.p. 160–162°, $[\alpha]_D^{21}$ +4·6° (c = 0·969), ν_{max}^{Nujol} 3556, 2166, 1724, 1266 cm^{-1}. (Found: C, 67·81; H, 8·74; N, 3·35; S, 7·92. $C_{22}H_{33}NO_3S$ requires: C, 67·48; H, 8·50; N, 3·58; S, 8·19%).

2β-*Thiocyanato*-3α-*mesyloxy*-5α-*androstan*-17β-*ol* 17-*acetate* (IId)

To a solution of IIc (2·735 g) in pyridine (20 ml) mesyl chloride (3·0 ml) was added under cooling. The reaction mixture was allowed to stand at 0° in a refrigerator overnight, poured into iced water, and extracted with ether–chloroform (3:1). The extract was washed successively with HCl aq, water, Na_2CO_3 solution, and then water, dried (Na_2SO_4), and evaporated to dryness. The residue was crystallized from ether to give the crystals (IId, 2·841 g, 86.6%), m.p. 150–154° (dec.). Two recrystallization from acetone–hexane afforded an analytical sample, m.p. 158–159° (dec), $[\alpha]_D^{16}$ +49·1° (c = 1·227), ν_{max}^{Nujol} 2154, 1735, 1336, 1245, 1174, 883 cm^{-1}. (Found: C, 59·00; H, 7·63; N, 3·20; S, 13·79. $C_{22}H_{35}NO_5S_2$ requires: C, 58·82; H, 7·51; N, 2·98; S, 13·66%).

17β-*Acetoxy*-5α-*androstan*-2β,3β-*episulphide* (IXb)

(a) Al_2O_3. The above IId (2·293 g) was dissolved in a mixture of pet. ether and benzene (4:1), absorbed over standardized Al_2O_3 (70 g), and allowed to stand for 2 days. Elution with benzene and crystallization from EtOH gave colorless plates (IXb, 1·407 g, 82·7%), m.p. 155–160°. Further recrystallization from ethanol afforded a pure sample m.p. 164–165°, $[\alpha]_D^{16}$ +21·4° (c = 1·094), λ_{max}^{alc} 263 mμ (ε 49), ν_{max}^{Nujol} 1730, 1247 cm^{-1}. (Found: C, 72·42; H, 9·23; S, 9·34. $C_{21}H_{32}O_2S$ requires: C, 72·36; H, 9·25; S, 8·20%).

(b) KOH-*diglyme*. The IId (966 mg) was dissolved in 5% KOH aq-*diglyme* (20 ml) and the resulting mixture was stirred at room temp for 2 days. After addition of water, the appeared precipitates

[26] J. Fajkoš and F. Šorm, *Coll. Czech. Chem. Comm.* **24**, 3115 (1959).

were collected by filtration, washed with water, dried, and recrystallized from ethanol to give IXb (502 mg), m.p. 158–160°. The mother liquor was evaporated to dryness and chromatographed over Al_2O_3 (2 g). Elution with 20% benzene–pet. ether afforded IXb, (53 mg), m.p. 162–164° (the combined yield of the episulphide: 77·2%).

2-Carbamoylimino[1,3]*oxathiolano compound* (XVI) *from the thiocyanatohydrin* (IIc)

A suspension of IIc (1·998 g) and Florisil (20 g) in benzene (200 ml) was stirred for 31 hr at room temp. The Florisil was removed by filtration and washed with benzene. The filtrate combined with washing was evaporated under red. press. The residue (660 mg) was chromatographed over Al_2O_3 (20 g) and elution with 20–40% benzene–pet. ether afforded IXb (413 mg, 23·3%), m.p. 164–165°. The Florisil was further washed with chloroform–methanol (1:1) and the solvent was removed. The residue (1·664 g) was recrystallized from methylene chloride–acetone to give the crystals (XVI, 716 mg, 32·7%), m.p. 255–256° (dec), $[\alpha]_D^{28}$ −6·7° (c = 1·032), ν_{max}^{Nujol} 3290, 3192, 1742, 1731, 1687, 1589, 1252 cm^{-1}. (Found: C, 63·70; H, 7·87; N, 6·65; S, 7·48. $C_{28}H_{34}N_2O_4S$ requires: C, 63·57; H, 7·98; N, 6·45; S, 7·36%).

Desulphurization of the carbamoylimino-oxathiolane (XVI)

A suspension of XVI (100 mg) and W-2 Raney nickel (1 ml) in dioxane (100 ml) was heated at 100° for 2·6 hr. After the Raney nickel was removed by filtration, the solvent was evaporated under red. press. The residue (89 mg) was chromatograhed over Al_2O_3 (3 g). Elution with 10–20% benzene–pet. ether afforded XVIIb (24 mg, 25·5%) as needles, m.p. 96–97°. Elution with 20% chloroform–benzene gave XVIII (18 mg), m.p. 183–185°, which was acetylated with pyridine and acetic anhydride to yield 3,17-diacetate, m.p. 155–157°. The IR spectra of both compounds were respectively in full agreement with those of the authentic samples.

3α-*Thiocyanato-5α-androstane-2β,17β-diol* 17-acetate (XIIa)

A solution of XIb (3·378 g, m.p. 170·5–172°, $[\alpha]_D^{25}$ −32·8° (c = 1·108) reported[27] m.p. 168·5–170°, $[\alpha]_D$ +35°) in ether (20 ml) was added to the thiocyanic acid solution prepared from KSCN (20 g), H_3PO_4 (30 g), and ether (30 ml) and allowed to stand for 2 days at room temp. The ethereal solution was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated to dryness. The residue was recrystallized from ether–hexane to give needles (XIIc, 3·821 g, 74·4%), m.p. 153–154°, $[\alpha]_D^{26}$ +30·4° (c = 1·071), ν_{max}^{Nujol} 3422, 2151, 1732, 1242, 1033 cm^{-1}. (Found: C, 67·26; H, 8·59; N, 3·95; S, 8·30. $C_{22}H_{33}NO_3S$ requires: C, 67·48; H, 8·50; N, 3·58; S, 8·19%).

2β-*Mesyloxy*-3α-*thiocyanato*-5α-*androstan*-17β-*ol acetate* (XIId)

To a solution of XIIc (2·619 g) in pyridine (26 ml) mesylchloride (2·6 ml) was added under cooling. The reaction mixture was allowed to stand overnight at room temp, poured into iced water, and extracted with ether. The ethereal solution was washed with HCl aq, water, Na_2CO_3 solution, and water, dried (Na_2SO_4), and evaporated. The residue was twice recrystallized from ether–pet. ether to yield XIId (1·799 g), m.p. 178–179°, $[\alpha]_D^{23·5}$ +24·9° (c = 0·536), ν_{max}^{Nujol} 2157, 1729, 1346, 1249, 1172 cm^{-1}. (Found: C, 58·87; H, 7·63; N, 3·22; S, 13·28. $C_{23}H_{35}NO_5S_2$ requires: C, 58·82; H, 7·51; N, 2·98; S, 13·66%).

17β-*Hydroxy*-5α-*androstan*-2α,3α-*episulphide* (XIVb)

Potassium hydroxide (1·2 g) was added to a solution of the crude XIId (1·20 g) in diglyme (24 ml). The resulting mixture was stirred for 42 hr at room temp, poured into water, and extracted with ether–chloroform (4:1). The extract was purified by chromatography over Al_2O_3 (30 g). Elution with pet. ether–benzene (1:1) gave XIVc (30 mg). The material (707 mg) eluted with pet. ether–benzene (1:1), benzene and benzene–chloroform (9:1–4:1) was recrystallized from acetone to yield XIVb (502 mg, 64·6%) as colorless plates, m.p. 127–128°, $[\alpha]_D^{27·5}$ −25·4° (c = 1·054), λ_{max}^{sic} 262 mμ (ε 51), ν_{max}^{Nujol} 3379, 1056, 1027, 957, 911 cm^{-1}. (Found: C, 73·58; H, 9·91; S, 10·35. $C_{19}H_{30}O_5 \cdot \frac{1}{2}H_2O$ requires: C, 73·37; H, 9·88; S, 10·31%). The XIVb was acetylated with pyridine and acetic anhydride to give XIVc, which was recrystallized from methanol to colorless plates, m.p. 144–145°,

[27] R. Kwok and M. Z. Wolff, *J. Org. Chem.* **28**, 423 (1963).

$[\alpha]_D^{28.5}$ +22·0° (c = 1·102), λ_{max}^{alc} 264 mμ (ε 53), $\nu_{max}^{CCl_4}$ 1735, 1243 cm⁻¹. (Found: C, 72·55; H, 9·24; S, 9·14. $C_{21}H_{32}O_2S$ requires: C, 72·36; H, 9·25; S, 9·20%).

17-Oxo-5α-androstan-2α,2α-episulphide (XIVd)

A solution of XIVb (1·061 g) in pyridine (25 ml) was added to the CrO_3–pyridine complex, prepared from pyridine (25 ml) and CrO_3 (1·00 g), and stirred overnight at room temp. After working up as usual, a neutral fraction (1·051 g) was obtained and chromatographed over Al_2O_3 (20 g). Elution with pet. ether–benzene (1:1) afforded a crude ketone (865 mg), which was recrystallized from methanol to give needles (XIVd, 654 mg, 62%), m.p. 107–108°, $[\alpha]_D^{27.5}$ +107·1° (c = 1·026), λ_{max}^{alc} 265 mμ (ε 59), 282·5 mμ (ε 50), ν_{max}^{Nujol} 1742 cm⁻¹. (Found: C, 74·64; H, 9·33; S, 10·42. $C_{19}H_{28}OS$ requires: C, 74·94; H, 9·21; S, 10·53%).

2-Carbamylimino[1,3]*oxathiolano compound* (XIX) *from the thiocyanatohydrin* (XIIc)

Florisil (17 g) was added to a solution of XIIc (1·667 g) in benzene (200 ml) and the mixture was stirred for 40 hr at room temp. Working up as mentioned above afforded XIVc (443 mg, 29·8%) and the urea compound, which was recrystallized from acetone to XIX (371 mg, 20·7%), m.p. 215–218°, $[\alpha]_D^{24}$ −9·9° (c = 1·004), λ_{max}^{alc} 247 mμ (ε 10100), ν_{max}^{Nujol} 3298, 3288, 1731, 1668, 1660, 1564, 1255 cm⁻¹. NMR: (18-H) 9·20τ; (19-H) 9·00; (OAc) 7·98; (NH_2) 4·24. (Found: C, 63·06; H, 7·88; N, 6·53; S, 7·55. $C_{23}H_{34}N_2O_4S$ requires: C, 63·57; H, 7·89; N, 6·45; S, 7·36%).

17β-Acetoxy-5α-androstane-2β,3α-dithiol trithiocarbonate (XXVIb)

(a) *From the 2β,3β-episulphide* (IXb). Carbon disulphide (12 ml) and IXb (1·407 g) were added to a solution of KOH (5 g) in methanol (30 ml), and the mixture was gently refluxed for 43 hr. To the yellow-colored reaction mixture water was added and extracted with chloroform. The chloroform solution was washed with water, dried (Na_2SO_4), and evaporated to dryness. The yellow residue was acetylated with pyridine (10 ml) and acetic anhydride (5 ml). The product (1·478 g) was chromatographed over Al_2O_3 (40 g). The material (946 mg) eluted with pet. ether–benzene (6:1–1:1) was crystallized from ether and further recrystallized from chloroform–ethanol to yield XXVIb (814 mg) as yellow plates, m.p. 209–211°, $[\alpha]_D^{24.5}$ +50·0° (c = 1·028), λ_{max}^{alc} 320 mμ (ε 16830), ν_{max}^{Nujol} 1730, 1251, 1112, 1066, 860 cm⁻¹. ORD: (c = 1·0276, $CHCl_3$), $[\alpha]_{479}$ +3416 (peak), $[\alpha]_{413}$ −7706 (trough), $[\alpha]_{396}$ −7552 (peak), $[\alpha]_{334}$ −24815 (trough), $[\alpha]_{290}$ +21409 (peak), $[\alpha]_{256}$ +3406 (trough). (Found: C, 62·05; H, 7·62; S, 22·54. $C_{22}H_{32}O_2S_3$ requires: C, 62·22; H, 7·60; S, 22·65%).

(b) *From the 2α,3α-episulphide* (XIVc). The XIVc (511 mg) was treated with a mixture of KOH (2·5 g), methanol (30 ml), and CS_2 (7 ml) as described above. After acetylation, the product was chromatographed over Al_2O_3 (15 g). Elution with pet. ether–benzene (6:1) gave 78 mg of 17β-acetoxy-5α-androst-2-ene, m.p. 98·5–100°. The material eluted with pet. ether–benzene (4:1–1:1) was recrystallized from chloroform–ethanol to yield the yellow XXVIb (278 mg), m.p. 209–211°. The IR spectrum of this compound was identical with that of the material described above.

17β-Hydroxy-5α-androstane-2β,3α-dithiol (XXVIIc)

To a stirred suspension of $LiAlH_4$ (390 mg) in tetrahydrofuran (10 ml), a solution of XXVIb (724 mg) in tetrahydrofuran (25 ml) was added dropwise over 10 min, and refluxed for 2 hr. The reaction mixture was cooled, poured into 5% HCl, and extracted with chloroform. The extract was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The residue (637 mg) was twice recrystallized from methanol to yield XXVIIc (505 mg) as colorless plates, m.p. 137–139°, $[\alpha]_D^{21}$ +33·7° (c = 1·085), ν_{max}^{Nujol} 3514, 2583, 1055 cm⁻¹. (Found: C, 67·14; H, 9·53; S, 18·83. $C_{19}H_{32}OS_2$ requires: C, 67·00; H, 9·47; S, 18·83%). This compound (138 mg) was acetylated with pyridine (1 ml) and acetic anhydride (1 ml) to give a triacetate, which was recrystallized from methanol to leaflets (XXVIId, 119 mg), m.p. 184–186°, $[\alpha]_D^{21}$ −23·8° (c = 1·079), λ_{max}^{alc} 232 mμ (ε 8940), ν_{max}^{Nujol} 1742, 1703 (sh), 1695, 1242, 1136, 1120 cm⁻¹. (Found: C, 64·66; H, 8·29; S, 13·63. $C_{25}H_{38}O_4S_2$ requires: C, 64·34; H, 8·21; S, 13·74%). A solution of XXVIIc (388 mg) and *p*-toluenesulphonic acid (40 mg) in acetone (10 ml) was refluxed for 7 hr, and poured into iced 5% Na_2CO_3 solution. The precipitate was collected by filtration, dried, and twice recrystallized from methanol to yield XXVIIIb (290 mg) as needles, m.p. 184–186°, $[\alpha]_D^{21}$ +61·8° (c = 1·122), $\nu_{max}^{CCl_4}$ 3628 1369 cm⁻¹. (Found: C, 69·15; H, 9·54; S, 16·89. $C_{22}H_{36}OS_2$ requires: C, 69·41; H, 9·53; S,

16·85%). This acetonide (213 mg) was acetylated with pyridine (2 ml) and acetic anhydride (1 ml) to give an acetoxy-acetonide, which was recrystallized from methanol to XXVIIIc (200 mg), m.p. 174–175°, $[\alpha]_D^{21}$ +53·0° (c = 1·112), ν_{max}^{Nujol} 1736, 1247, 1359 cm^{-1}. (Found: C, 68·22; H, 9·12; S, 15·10. $C_{34}H_{58}O_2S_2$ requires: C, 68·19; H, 9·06; S, 15·17%).

6β-Mercapto-5α-cholestane-3β,5α-diol triacetate (XXI)

To a solution of XX[20] (1·350 g) in a mixture of acetic acid (25 ml) and acetic anhydride (10 ml), *p*-toluenesulphonic acid (800 mg) was added under cooling. The reaction mixture was allowed to stand overnight at room temp, poured into iced water, and extracted with ether–chloroform (3:1). The extract was washed with water, Na_2CO_3 solution, and water, dried (Na_2SO_4), and evaporated. The residue was twice recrystallized from aqueous acetone to give XXI (1·070 g) as prisms, m.p. 165–167°, $[\alpha]_D^{22}$ −48·1° (c = 0·982), λ_{max}^{alc} 232 mμ (ε 4730), 306 mμ (ε 490), ν_{max}^{Nujol} 1728, 1689, 1247, 1231, 1035 cm^{-1}. (Found: C, 70·36; H, 9·64; S, 5·94. $C_{33}H_{54}O_6S$ requires: C, 70·42; H, 9·67; S, 5·70%).

3β-Hydroxycoprostan-5β,6β-episulphide (XXII)

To a solution of XXI (1·070 g) in absolute ethanol (40 ml) KOH (1·50 g) was added and the mixture was refluxed for 1 hr. The mixture was cooled, poured into water, and extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated. The product was twice recrystallized from methanol to yield XXII (627 mg) as needles, m.p. 112–113°, $[\alpha]_D^{22}$ +16·0° (c = 1·007), λ_{max}^{alc} 263 mμ (ε 46), ν_{max}^{Nujol} 3290–3250, 1039, 1023 cm^{-1}. (Found: C, 77·77; H, 11·20; S, 7·70. $C_{27}H_{46}OS$ requires: C, 77·45; H, 11·07; S, 7·66%).

Reduction of episulphides

(i) *Cholestan-2β,3β-episulphide* (IXa). (a) To a stirred suspension of $LiAlH_4$ (205 mg) in ether (20 ml) a solution of IXa, (1·430 g) in tetrahydrofuran (30 ml) was added and stirred under reflux for 1·5 hr. The mixture was poured into iced 5% HCl and extracted with ether. The extract was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The product was chromatographed over Al_2O_3 (35 g). Elution with pet. ether afforded XVIIa (295 mg, 22·4%), m.p. 73–74°. Further elution with pet. ether–benzene afforded a gel, which could not be separated.

(b) To a stirred suspension of $LiAlH_4$ (190 mg) in ether (20 ml) a solution of IXa (1·360 g) in tetrahydrofuran (20 ml) was added and the mixture was stirred under reflux for 1·5 hr. The product was acetylated with pyridine (5 ml) and acetic anhydride (3 ml). The acetylation product was recrystallized from pentane and further from acetone to yield XXIIIa (697 mg) as colorless leaflets, m.p. 160–162°, $[\alpha]_D^{22}$ +3·9° (c = 0·985), λ_{max}^{alc} 234 mμ (ε 5660), ν_{max}^{Nujol} 1688, 1138, 1120, 958 cm^{-1}. (Found: C, 78·04; H, 11·30; S, 7·23. $C_{29}H_{50}OS$ requires: C, 77·96; H, 11·28; S, 7·18%). The mother liquor was evaporated and the residue (605 mg) was chromatographed over Al_2O_3 (18 g). Elution with pet. ether afforded XVIIa (203 mg, 16%), m.p. 72–73°. Elution with pet. ether containing 5%–50% benzene gave a gel (231 mg), which was not further studied. Elution with benzene afforded the 2β-acetylthio compound (216 mg), m.p. 154–158° (the combined yield of the acetylthio compound (XXIIIa, 913 mg, 60%). This acetylthio compound (142 mg) was reduced with $LiAlH_4$ (18 mg) in ether (10 ml) for 15 min at 0°. The product was recrystallized from acetone to yield XXIIIb (105 mg) as fine needles, m.p. 95·5–96·5°, $[\alpha]_D^{25.5}$ +16·6° (c = 1·018). (Found: C, 80·16; H, 11·98; S, 8·24. $C_{27}H_{48}S$ requires: C, 80·12; H, 11·95; S, 7·92%).

(ii) *Cholestan-2α,3α-episulphide* (XIVa). (a) A suspension of $LiAlH_4$ (180 mg) and XIVa (1·470 g) in a mixture of ether (20 ml) and tetrahydrofuran (20 ml) was stirred under reflux for 1·5 hr. The product was recrystallized from acetone to yield the recovered episulphide (905 mg, 61·5%), m.p. 119–121°. Chromatography of the mother liquor afforded only isolatable 5α-cholest-2-ene (229 mg, 16·9%), m.p. 72–73°.

(b) A suspension of $LiAlH_4$ (500 mg) and XIVa (500 mg) in tetrahydrofuran (30 ml) was stirred for 2 hr at room temp and then refluxed for 1 hr. The product (472 mg) was chromatographed over Al_2O_3 (30 g). Elution with pet. ether afforded 5α-cholest-2-ene (172 mg, 37·4%), m.p. 73–74°. The material eluted with pet. ether–benzene (4:1) was recrystallized from ethyl acetate to yield XXIV (26 mg), m.p. 175–177°, $[\alpha]_D^{19.5}$ +24·9° (c = 1·00), λ_{max}^{alc} 206 mμ (ε 2690), 250 mμ (ε 440). (Found: C, 80·24; H, 11·78; S, 7·96. $C_{54}H_{94}S_2$ requires: C, 80·32; H, 11·74; S, 7·93%). The material

(89 mg) eluted with pet. ether–benzene (1:1), benzene, and with benzene–chloroform (9:1–1:1) was oxidized with I_2 (31 mg) in hexane-ethanol to give the disulphide (55 mg), m.p. 175–177° (the combined yield of the disulphide (XXIV, 16·2%). This disulphide (298 mg) was reduced with $LiAlH_4$ in ether, followed by acetylation, to give XXVa (116 mg), m.p. 119–120°.

(c) A suspension of $LiAlH_4$ (175 mg) XIVa (1·374 g) in tetrahydrofuran (45 ml) was stirred under reflux for 3 hr. The product was acetylated with pyridine (6 ml) and acetic anhydride (4 ml). The acetylation product (1·445 g) was chromatographed over Al_2O_3 (42 g). Elution with pet. ether afforded 5α-cholest-2-ene (532 mg, 42%). Further elution with pet. ether gave a mixture (213 mg). The material (655 mg) eluted with pet. ether–benzene (9:1) was recrystallized from acetone to yield XXVa (608 mg, 40%), m.p. 119·5–120·5°, $[\alpha]_D^{28\cdot5}$ +38·2° (c = 1·00), ν_{max}^{Nujol} 1691, 1137, 1109 cm^{-1}. (Found: C, 77·94; H, 11·21; S, 7·38. Calc. for $C_{29}H_{50}OS$: C, 77·96; H, 11·28; S, 7·18%). Reported[28] m.p. 121°, $[\alpha]_J$ +43°. This acetylthio compound (405 mg) was reduced with $LiAlH_4$ (40 mg) in ether (20 ml) for 1 hr at 0°. The product was recrystallized from acetone to give XXVb (350 mg), m.p. 82–83°, $[\alpha]_D^{28\cdot5}$ +31·1° (c = 1·00), λ_{max}^{alc} 207 mμ (ε 670). (Found: C, 80·13; H, 11·97; S, 7·77. Calc. for $C_{27}H_{48}S$: C, 80·12; H, 11·95; S, 7·92%). Reported[28] m.p. 81°, $[\alpha]_J$ +32°. By mixed m.p. and comparison of the IR spectra, this compound was identical with the authentic sample, prepared from 3α-thiocyanato-5α-cholestane,[10,11] m.p. 89–90°, $[\alpha]_D^{25\cdot5}$ +31·1°, ν_{max}^{Nujol} 2182 cm^{-1}. (Found: C, 78·59; H, 11·03; N, 3·52; S, 7·54. Calc. for $C_{28}H_4$-NS: C, 78·27; H, 11·03; N, 3·26; S, 7·45%).

(iii) *17β-Acetoxy-5α-androstan-2β,3β-episulphide* (IXb). (a) A stirred suspension of IXb (504 mg) and $LiAlH_4$ (250 mg) in tetrahydrofuran (28 ml) was refluxed for 3 hr. The product was acetylated by pyridine (5 ml) and acetic anhydride (5 ml). The acetylation product (557 mg) was chromatographed over Al_2O_3 (33 g). Elution with pet. ether–benzene (9:1) afforded XVIIb (117 mg, 25·5%), m.p. 97–98°. The material eluted with pet. ether–benzene (4:1–1:1) was recrystallized from methanol to yield XXIIIc (283 mg, 56·6%), m.p. 171–173°, $[\alpha]_D^{22\cdot5}$ −21·3° (c = 0·883), λ_{max}^{alc} 234 mμ (ε 5240), $\nu_{max}^{CCl_4}$ 1738, 1248, 1691, 1118 cm^{-1}. NMR: (18-H) 9·23τ; (19-H) 9·10; (OAc) 8·00; (SAc) 7·62. (Found: C, 70·52; H, 9·26; S, 8·38. $C_{32}H_{56}OS$ requires: C, 70·37; H, 9·24; S, 8·15%).

(b) Reduction of IXb (303 mg) with $LiAlH_4$ (60 mg) in a mixture of ether (9 ml) and tetrahydrofuran (9 ml), provided 45 mg (15%) of 17β-acetoxy-5α-androst-2-ene and 135 mg (45%) of the recovered episulphide.

3α-*Thiocyanato-5α-cholestan-4β-ol* XXXIIa)

To a solution of thiocyanic acid in ether (15 ml), prepared from KCNS (4 g), XXXI[22] (m.p. 93–95°, 836 mg) was added and the resulting mixture was allowed to stand overnight at room temp. The mixture was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The residual solid was recrystallized from hexane to yield XXXIIa (806 mg) as needles, m.p. 170–172° $[\alpha]_D^{25}$ +40·2° (c = 1·061), ν_{max}^{Nujol} 3544, 2152 cm^{-1}. NMR: (18-H) 9·37τ; (19-H) 8·98; (3β-H and 4α-H) 6·19 (W_H 7·0 c/s). (Found: C, 75·37; H, 10·69; N, 3·32; S, 7·28. $C_{28}H_{47}NOS$ requires: C, 75·44; H, 10·63; N, 3·14; S, 7·19%). This compound (347 mg) was acetylated with pyridine and acetic anhydride to give an acetate, which was recrystallized from methylene chloride–methanol to XXXIIb (360 mg), m.p. 162–163°, $[\alpha]_D^{25}$ −8·2° (c = 1·011), ν_{max}^{Nujol} 2153, 1740, 1248 cm^{-1}. NMR: (18-H) 9·37τ; (19-H) 9·00; (3β-H) 6·19 (W_H 7·0 cps); (4α-H) 5·08 (W_H 5·0); (OAc) 7·95. (Found: C, 73·63; H, 9·99; N, 2·83; S, 6·91. $C_{30}H_{49}NO_2S$ requires: C, 73·87; H, 10·13; N, 2·87; S, 6·57%).

Desulphurization of the thiocyanatohydrin acetate (XXXIIb)

To a solution of XXXIIb (210 mg) in ethanol (8 ml), W-2 Raney Ni (2 ml) was added and the mixture was refluxed for 10 hr. After Raney Ni was removed by filtration, the solution was poured into water, and extracted with ether. The extract was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The residue was three times recrystallized from ethanol to give XXXIII (40 mg), m.p. 79–80°. The mother liquor was evaporated to dryness and the residue was chromatographed over Al_2O_3 (4 g). Elution with pet. ether afforded further 5α-cholestane (57 mg), m.p. 79–80° (the combined yield of 5α-cholestane, 63%). The material (48 mg) eluted with pet. ether containing

[28] R. Bourdon, *Bull. Soc. Chim. Fr.* 844 (1962).

5% and 10% benzene was recrystallized from ether–methanol to yield XXXIV (19 mg, 13%), m.p. 104·5–105·5°, which showed the identical IR spectrum with that of the authentic sample.[28]

5α-Cholestan-3α,4α-episulphide (XXXV)

To a solution of KOH (1·0 g) in absolute ethanol (20 ml), XXXIIb (307 mg) was added. The mixture was refluxed for 1 hr, poured into water, and extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated. The residue was dissolved in pet. ether and chromatographed over Al_2O_3 (4·0 g). The material eluted with pet. ether and 5% benzene–pet. ether was recrystallized from acetone to yield XXXV (178 mg) as colorless needles, m.p. 120–121°, $[\alpha]_D^{25}$ +39·7° (c = 1·053). ORD: (c = 0·2005, dioxane), $[\phi]_{700}$ +40, $[\phi]_{270}$ +4600 (peak), $[\phi]_{255}$ −5500 (trough), $[\phi]_{215}$ −4360. NMR: (18-H) 9·35τ; (19-H) 9·19; (3β-H) 6·81; (4β-H) 7·41; $J_{3\beta-H:4\beta-H}$ = 6·5 c/s; $J_{3\beta-H:2\alpha\ H}$ = $J_{3\beta-H:2\beta-H}$ = 3·0; $J_{4\beta-H:5\alpha-H}$ = 3·0. (Found: C, 80·68; H, 11·48; S, 7·86. $C_{27}H_{46}S$ requires: C, 80·52; H, 11·51; S, 7·96%).

Reduction of the episulphide (XXXV)

(a) *With Raney nickel.* To a solution of XXXV (33 mg) in ethanol (5 ml) W-2 Raney Ni (0·5 ml) was added and the mixture was refluxed for 8 hr. Raney Ni was removed by filtration and washed with ether. The filtrate combined washing was evaporated and recrystallized from ethanol to yield XXXIII (24 mg), m.p. 80–81°, which was identified by mixed m.p. and comparison of the IR spectra.

(b) *With zinc-acetic acid.* To a solution of XXXV (27 mg) in acetic acid (3 ml) Zn dust (500 mg) was added. The resulting mixture was stirred under reflux for 3 hr, cooled, poured into water, and extracted with ether. The ethereal solution was washed with water, Na_2CO_3 solution, and water, and evaporated. The residue was recrystallized from acetone to yield XXXVI (18 mg), m.p. 72–74°, which was identical with the authentic sample by mixed m.p. and comparison or the IR spectra.

4β-Thiocyanato-5α-androstane-3α,17β-diol 17-acetate (XXXVIIIc)

Compound XXXVIIb (1·023 g) was added to thiocyanic acid–ether solution (30 ml), prepared from KCNS (6·0 g), and the mixture was allowed to stand overnight at room temp. The ethereal solution was washed with Na_2CO_3 and water, dried (Na_2SO_4), and evaporated. The residue was recrystallized from ether–pet. ether and further from acetone–hexane to yield XXXVIIIc (800 mg) as colorless leaflets, m.p. 192–194°, $[\alpha]_D^{25.5}$ +1·9° (c = 0·963), ν_{max}^{Nujol} 3523, 2169, 1733, 1239, 1039 cm^{-1}. (Found: C, 67·78; H, 8·50; N, 3·63; S, 8·07. $C_{22}H_{33}NO_3S$ requires: C, 67·48; H, 8·50; N, 3·58; S, 8·19%). An attempted direct conversion of this compound to an episulphide failed. The XXXVIII (100 mg) was heated for 1 hr in 5% KOH–methanol (10 ml) and the product was acetylated to give XXXVIIb (40 mg), m.p. 186–187°, which was identified by mixed m.p. and comparison of the IR spectra. The XXXVIIIc (800 mg) was mesylated with mesylchloride (10 ml) and pyridine (20 ml). The product was recrystallized from acetone–hexane to give XXXVIIId (964 mg) as fine needles, m.p. 183–184°, $[\alpha]_D^{21.5}$ −25·3° (c = 1·026), ν_{max}^{Nujol} 2163, 1726, 1243, 1352, 1183 cm^{-1}. (Found: C, 58·95; H, 7·31; N, 3·15; S, 13·97. $C_{23}H_{35}NO_5S_2$ requires: C, 58·82; H, 7·51; N, 2·98; S, 13·66%).

17β-Hydroxy-5α-androstan-3β,4β-episulphide (XXXIXc)

The XXXVIIId (200 mg) was dissolved in a solution of KOH (200 mg) in diglyme (6 ml) and the resulting mixture was stirred for 41 hr at room temp. The mixture was poured into water and extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated. The product (120 mg) was chromatographed over Al_2O_3 (3·6 g) and the material eluted with benzene was recrystallized from acetone to give XXXIXc as colorless needles, m.p. 172–173°. (Found: C, 74·31; H, 10·00; S, 10·15. $C_{19}H_{30}OS$ requires: C, 74·47; H, 9·87; S, 10·44%). This compound was acetylated with pyridine and acetic anhydride to yield XXXIXb which was recrystallized from acetone to flat needles, m.p. 179–180°, $[\alpha]_D^{21}$ +30·2° (c = 1·011), ν_{max}^{Nujol} 1734, 1252, 1049, 1034 cm^{-1}. (Found: C, 72·55; H, 9·23; S, 9·02. $C_{21}H_{32}O_2S$ requires: C, 72·36; H, 9·25; S, 9·20%). This acetate was also obtained directly from XXXVIIId. The mesylate (510 mg) was dissolved in pet. ether–benzene (1:1), absorbed over a column of standardized Al_2O_3 (15 g) and allowed to stand for 2 days at room temp. Elution with the same solvent afforded the acetate, which was recrystallized from acetone to XXXIXb (200 mg), m.p. 179–180°.

[28] A. Fürst, H. H. Kuhn, R. Scotoni, Jr. and H. H. Günthard, *Helv. Chim. Acta* **35**, 951 (1952).

4β-Thiocyanato-5α-cholestan-3α-ol (XXXVIIIa)

Compound XXXVIIa (1·519 g) was dissolved in a solution of thiocyanic acid in ether (80 ml), prepared from KCNS (13 g), and left to stand overnight at room temp. The product was recrystallized from acetone to yield XXXVIIIa (1·339 g), m.p. 158–160°, $[\alpha]_D^{19}$ + 27·0° (*c* = 1·056), ν_{max}^{Nujol} 3466, 2162 cm^{-1}. (Found: C, 75·53; H, 10·61; N, 3·15; S, 7·35. $C_{28}H_{47}NOS$ requires: C, 75·44; H, 10·63; N, 3·14; S, 7·19%). This compound was acetylated with pyridine and acetic anhydride to give XXXVIIIb, which was recrystallized from ethanol to plates, m.p. 162–164°, $[\alpha]_D^{20}$ − 0·8°, ν_{max}^{Nujol} 2158, 1743, 1243 cm^{-1}. (Found: C, 73·58; H, 10·10; S, 6·57; $C_{30}H_{49}NO_2S$ requires: C, 73·88; H, 10·13; S, 6·56%).

4β-Mercapto-5α-cholestan-3α-ol (XLa)

To a stirred suspension of $LiAlH_4$ (200 mg) in ether (15 ml), a solution of XXXVIIIa (1·00 g) in ether (15 ml) was added dropwise and the mixture was stirred under reflux for 1 hr. The product (918 mg) was recrystallized from acetone to yield XLa (896 mg), m.p. 161–163°, $[\alpha]_D^{23·5}$ + 35·3° (*c* − 0·985). (Found: C, 76·95; H, 11·46; S, 7·63. $C_{27}H_{48}OS$ requires: C, 77·08; H, 11·50; S, 7·62%). This compound was acetylated by pyridine and acetic anhydride to give an oily XLb, which could not be crystallized. The attempted conversions of XLa to 2-substituted [1,3]oxathiolano compounds were unsuccessful: (a) Refluxing of a solution of XLa and *p*-toluenesulphonic acid in acetone for 34 hr afforded no acetonide (T.L.C.); (b) Refluxing of a solution of XLa and N,N′-thiocarbonylbis(2-methylimidazol) in chloroform for 14 hr gave no dithiocarbonate.

5α-Cholestan-3β,4β-episulphide (XXXIXa)

The XXXVIIIa (300 mg) was mesylated with mesylchloride (0·3 ml) and pyridine (5 ml) at 0°. The crude mesylate (255 mg), which was not purified, was dissolved in pet. ether–benzene (9:1), absorbed over a column of standardized Al_2O_3 (7·5 g), and left to stand overnight at room temp. The material (139 mg) eluted with pet. ether–benzene (9:1–4:1) was recrystallized from ethanol to give XXXIXa (109 mg), m.p. 136–138°, $[\alpha]_D^{24·5}$ + 53·1° (*c* = 1·860). (Found: C, 80·22; H, 11·67; S, 7·84. $C_{27}H_{46}S$ requires: C, 80·52; H, 11·51; S, 7·96%).

Oxidation of the thiocyanatohydrin (XXXVIIIa)

(a) To a stirred solution of XXXVIIIa (1·057 g) in purified acetone (75 ml) Jones reagent (1·05 equiv) was added. The reaction mixture was stirred for 10 min, poured into water, and extracted with methylene chloride. The extract was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The residue (1·089 g) was twice recrystallized from acetone to yield XLI (853 mg), m.p. 145–147°, $[\alpha]_D^{24·5}$ −11·0° (*c* = 0·980), $\nu_{max}^{CCl_4}$ 2156, 1727 cm^{-1}. ORD: (*c* = 0·1085, dioxane), $[\alpha]_{700}$ −37, $[\alpha]_{331·5}$ −995 (trough), $[\alpha]_{284}$ + 1493 (peak), $[\alpha]_{255}$ +1032. NMR: (18-H) 9·34τ; (19-H) 8·95; (4α-H) 6·26[30]; $J_{4\alpha-H\,:\,5\alpha-H}$ = 4·5 c/s. (Found: C, 76·10; H, 10·26; S, 7·21. $C_{28}H_{46}NOS$ requires: C, 75·80; H, 10·22; S, 7·21%).

(b) The XXXVIIIa (1·868 g) was oxidized with Jones reagent (1·5 equiv) in acetone (150 ml) for 1 hr. The product was recrystallized from acetone to give XLII (1·170 g), m.p. 166–168°, $[\alpha]_D^{24}$ +41·8° (*c* = 1·088), $\nu_{max}^{CCl_4}$ 2161, 1726 cm^{-1}. ORD (*c* = 0·2369, dioxane), $[\alpha]_{700}$ +42, $[\alpha]_{304}$ +836 (peak), $[\alpha]_{262}$ −886 (trough), $[\alpha]_{245}$ −245. NMR: (18-H) 9·33τ; (19-H) 8·88; (4β-H) 6·02; $J_{4\beta-H\,:\,5\alpha-H}$ = 11·5 c/s. (Found: C, 75·65; H, 10·38; S, 7·32. $C_{28}H_{46}NOS$: C, 75·80; H, 10·22; S, 7·21%).

(c) The XXXVIIIa (1·150 g) was oxidized with Jones reagent (1·05 equiv.) in acetone (80 ml) for 30 min. The product was recrystallized from acetone to yield XLI (290 mg), m.p. 140–142°, and XLII (14 mg), m.p. 166–168°. The mother liquor was evaporated and chromatographed over Al_2O_3 (18 g). Elution with pet. ether–benzene (9:1–1:1) afforded an oily substance (94 mg), which was not further studied. The material (499 mg) eluted with benzene–ether (95:5–9:1) was recrystallized from chloroform–methanol to yield XLIII (260 mg), m.p. 285–288° (dec), $[\alpha]_D^{24·5}$ +42·3° (*c* = 1·021), λ_{max}^{alc} 252 mμ (ε 5760), ν_{max}^{Nujol} 3145, 3030, 1680 cm^{-1}. (Found: C, 75·41; H, 10·24; N, 3·28; S, 7·25. $C_{28}H_{45}NOS$ requires: C, 75·80; H, 10·22; N, 3·61; S, 7·21%).

[30] In this case 4α-proton (eq.) of XLI appeared at higher field by 0·24 ppm than 4β-proton (ax.) of XLII. (cf. K. M. Wellman and F. G. Bordwell, *Tetrahedron Letters* 1703 (1963). A. Nickon, M. A. Castle, R. Harada, C. E. Benkoff and R. O. Williams, *J. Amer. Chem. Soc.* **85**, 2185 (1963).

(d) Epimerization of the 4β-thiocyanato-3-one to the 4α-thiocyanato-3-one. The XLI (328 mg) was dissolved in a solution of thiocyanic acid in chloroform[80,81] (0·78 M) and left to stand for 2 days at room temp. The solution was washed with Na_2SO_3 solution and water, dried (Na_2SO_4), and evaporated. The residue (322 mg) was recrystallized from acetone to yield XLII (40 mg), m.p. 163–166°. The mother liquor was evaporated and then chromatographed over silica gel (8 g). Elution with pet. ether–benzene (9:1–1:1) afforded an oily substance (62 mg). The material (114 mg) eluted with pet. ether–benzene (3:7) and benzene was recrystallized from acetone to give XLII (72 mg), m.p. 164–167° (the combined yield of the 4α-thiocyanato-3-one, 112 mg).

Reduction of the 4α-thiocyanato-3-one (XLII) *with lithium aluminum hydride*

(a) 4α-*Mercapto-5α-cholestan-3α-ol* (XLIVa). To a stirred suspension of $LiAlH_4$ (238 mg) in ether (10 ml), a solution of XLII (697 mg) in ether (30 ml) was added dropwise under cooling and stirred for 1·5 hr at room temp. To the reaction mixture, iced 5% HCl was added and extracted with ether. Th extract was washed with Na_2CO_3 solution and water, dried (Na_2SO_4), and evaporated. The residue (620 mg) was chromatographed over Florisil (19 g). The crystals (153 mg) eluted with pet. ether–benzene (1:2–1:3) was recrystallized from acetone–hexane to yield XLIVa (135 mg, 20·4%), m.p. 139–141°, $[\alpha]_D^{28}$ −19·5° (c = 1·044). (Found: C, 77·11; H, 11·48; S, 7·87. $C_{27}H_{46}OS$ requires: C, 77·08; H, 11·50; S, 7·62%). This compound was acetylated with pyridine and acetic anhydride and the product was recrystallized from acetone to give XLIVb, m.p. 136–138°, $[\alpha]_D^{28}$ −31·3° (c = 1·036), $\nu_{max}^{CCl_4}$ 1740, 1699, 1240, 1214 cm^{-1}. (Found: C, 74·03; H, 10·39; S, 6·56. $C_{31}H_{52}O_3S$ requires: C, 73·96; H, 10·30; S, 6·30%). A solution of XLIVa (108 mg) and *p*-toluenesulphonic acid (15 mg) in acetone (23 ml) was heated under reflux for 6·5 hr, cooled, poured into iced Na_2CO_3 solution, and extracted with ether. The product (120 mg) was dissolved in pet. ether and passed through a column of Al_2O_3 (3·5 g). The product (97 mg) was recrystallized from acetone to yield XLVIa (87 mg), m.p. 138–140°. (Found: C, 78·26; H, 11·29; S, 6·82. $C_{30}H_{52}OS$ requires: C, 78·20; H, 11·37; S, 6·96%). A solution of XLIVa (67 mg) and N,N′-thiocarbonylbis(2-methylimidazol) (40 mg) in chloroform (6 ml) was heated under reflux for 4·5 hr. The product (72 mg) was chromatographed over Al_2O_3 (2 g). The material (45 mg) was recrystallized from acetone to yield XLVIb (34 mg), m.p. 229–232°, λ_{max}^{alc} 281 mμ (ε 10230), 369 mμ (ε 54), $\nu_{max}^{CCl_4}$ 1212, 1190 cm^{-1}. (Found C, 72·88; H, 10·07; S, 13·61. $C_{35}H_{64}OS_2$ requires: C, 72·69; H, 10·02; S, 13·83%).

(b) 4α-*Mercapto-5α-cholestan-3β-ol* (XLVa). On the chromatography described in (a), further elution with benzene and benzene–ether (95:5–9:1) afforded a mixture of crystals (353 mg), which were acetylated with pyridine (4 ml) and acetic anhydride (2 ml). The product (460 mg) was chromatographed over Al_2O_3 (9·5 g). Elution with pet. ether gave 5α-cholestan-3β-ol acetate (38 mg, 6·2%). The material eluted with pet. ether–benzene (9:1–7:3) was recrystallized from acetone to yield XLVb (329 mg, 41·3%), m.p. 143–145°, $[\alpha]_D^{28}$ +9·8° (c = 1·122), $\nu_{max}^{CCl_4}$ 1742, 1695, 1240 cm^{-1}. (Found: C, 74·12; H, 10·39; S, 6·51. $C_{31}H_{52}O_3S$ requires: C, 73·96; H, 10·30; S, 6·30%). This compound (309 mg) was reduced with $LiAlH_4$ (104 mg) in ether (21 ml) at 5° for 1 hr. The product (260 mg) was recrystallized from acetone to yield the XLVa (232 mg), m.p. 163–165°, $[\alpha]_D^{25}$ −5·4° (c = 1·023). (Found: C, 77·24; H, 11·52; S, 7·66. $C_{27}H_{48}OS$ requires: C, 77·08; H, 11·50; S, 7·62%). A solution of XLVa (150 mg) and *p*-toluenesulphonic acid (20 mg) in acetone (30 ml) was heated under reflux for 6 hr. The product (182 mg) was chromatographed over Al_2O_3 (5 g). The material eluted with pet. ether was recrystallized from acetone to yield XLVIIa (54 mg), m.p. 172–174°. (Found: C, 78·29; H, 11·34; S, 7·13. $C_{30}H_{52}OS$ requires: C, 78·20; H, 11·37; S, 6·96%). A solution of XLVa (58 mg) and N,N′-thiocarbonylbis(2-methylimidazol) (35 mg) in chloroform (5 ml) was heated under reflux for 2·5 hr. The product (56 mg) was purified by chromatography over Al_2O_3 to give a dithiocarbonate, which was recrystallized from acetone to XLVIIb (35 mg), m.p. 145–148°, λ_{max}^{alc} 284 mμ (ε 18200), 374 mμ (ε 100), $\nu_{max}^{CCl_4}$ 1200 cm^{-1}. (Found: C, 72·54; H, 10·18. $C_{58}H_{46}OS_2$ requires: C, 72·69; H, 10·02%).

An attempted conversion of episulphides to trithiocarbonates

(a) 3β-*Hydroxycholestan-5α,6α-episulphide*. Carbon disulphide (12 ml) and 3β-Hydroxy-cholestan-5α,6α-episulphide[20] (1·748 g) were added to a solution of KOH (5 g) in methanol (30 ml). The reaction mixture was heated under reflux for 43 hr. The product (1·40 g), isolated by extraction with

[81] K. Takeda, T. Kubota and J. Kawanami, *Chem. Pharm. Bull., Japan* **8**, 615 (1960).

ether, was acetylated with pyridine and acetic anhydride to yield a material (1·70 g), which was chromatographed over Al_2O_3 (47 g). Elution with pet. ether and pet. ether–benzene (9:1) afforded crystals (1·465 g), which were recrystallized from MeOH to give cholesterylacetate (1·22 g, 68·2%), m.p. 110–112°. Further elution did not yield a yellow trithiocarbonates.

(b) *3β-Hydroxycholestan-5β,6β-episulphide.* A similar treatment of the 5β,6β-episulphide (441 mg), as described above afforded also cholesterol (52·4%) and the unreacted episulphide (23·6%).

(c) *3.3-Ethylenedioxypregn-5-en-16β,17β-episulphide.*[32] A similar treatment of the 16β,17β-episulphide (706 mg) as described above gave the unreacted episulphide (586 mg, 83·0%), m.p. 202–203° (dec).

(d) A similar treatment of both 5α-cholestan-3α,4α- and 3β,4β-episulphide as described above gave no trithiocarbonate besides 5α-cholest-3-ene and the starting materials (T.L.C.).

[32] K. Takeda and T. Komeno, to be published.