Steroidal Sulphur Compounds. Part XI.[1] 4-Thia-5α- and 5β-Cholestane and their Oxides and Dioxides

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Cholesterol was converted in nine steps into 4-thia-5β-cholestane in 36% overall yield. The final step involved the intramolecular addition of a thio-radical, generated photocatalytically from A-nor-3,5-secocholest-5-ene-3-thiol, to the double bond to give 4-thia-5β-cholestane stereospecifically. Another approach involved the intramolecular addition of a sulphenic acid, generated by pyrolysis of 3-t-butylsulphinyl-A-nor-3,5-secocholest-5-ene, to the double bond to give 4-thia-5β-cholestane 4α-oxide stereospecifically. Base-catalysed isomerisation of 4-thia-5β-cholestane 4,4-dioxide and 4-thia-5β-cholestane 4α-oxide gave 4-thia-5α-cholestane 4,4-dioxide and 4-thia-5α-cholestane 4α-oxide quantitatively, whereas 4-thia-5β-cholestane 4β-oxide gave a *ca.* 56 : 44 mixture of starting material and 4-thia-5α-cholestane 4β-oxide. Reduction of 4-thia-5α-cholestane 4β-oxide gave 4-thia-5α-cholestane. The oxides were configurationally stable at 190°, but underwent photocatalysed stereomutation at sulphur without concomitant isomerisation at C-5.

INTEREST in the potential physiological activity and physicochemical properties of thia-steroids has motivated the synthesis of steroidal derivatives in which the carbon atoms at position 2,[2] 3,[3] 6,[4,5] and 7,[5] have been replaced by a sulphur atom. We required 4-thia-5β-cholestane (I), 4-thia-5α-cholestane (II), and their oxides for mechanistic studies, and this paper describes their synthesis.

Preliminary experiments showed that the usual method of constructing thian rings [2,3,6,7] was not appropriate for the synthesis of the steroidal thians (I) and (II). The Windaus keto-acid (III), obtained readily in two steps from cholesterol, was reduced by lithium aluminium hydride to the diols (IV) and (V),[8] which were separated chromatographically and treated with methanesulphonyl chloride. The complexity of the mixtures of products (according to t.l.c.) obtained when the bismethanesulphonates (VI) and (VII) were treated with anhydrous sodium sulphide, or its nonahydrate, in ethanol, dimethyl sulphoxide, hexamethylphosphoramide, or *N*-methyl-2-pyrrolidone, indicated that these reactions would not provide a practical synthesis of the cyclic sulphides (I) and (II). In a modified approach the bismethanesulphonates (VI) and (VII) were converted into the thioacetoxy-methanesulphonates (VIII) and (IX), respectively, by selective reaction of the primary methanesulphonate group with tetrabutylammonium thioacetate in acetone. Compound (IX) was treated with lithium aluminium hydride to give the mercapto-methanesulphonate (X), which with sodium

[1] Part X, D. N. Jones, J. Blenkinsopp, A. C. F. Edmonds, E. Helmy, and R. J. K. Taylor, *J.C.S. Perkin I*, 1974, 937.

[2] (*a*) Y. Kashman and E. D. Kaufman, *Tetrahedron*, 1971, **27**, 3437; (*b*) P. B. Sollman, R. Nagarajan, and R. M. Dodson, *Chem. Comm.*, 1967, 552.

[3] R. Nagarajan, B. H. Chollar, and R. M. Dodson, *Chem. Comm.*, 1967, 550; D. Gust, J. Jacobus, and K. Mislow, *J. Org. Chem.*, 1968, **33**, 2996; D. Bertin and J. Perronnett, *Bull. Soc. chim. France*, 1968, 1422.

[4] R. B. Mitra and B. D. Tilak, *J. Sci. Ind. Res., India*, 1956, **15B**, 573; R. J. Collins and E. V. Brown, *J. Amer. Chem. Soc.*, 1957, **79**, 1103; J. G. Westra, W. N. Speckamp, U. K. Pandit, and H. P. Huisman, *Tetrahedron Letters*, 1966, 2781; W. M. B. Konst, J. L. Van Bruynsvoort, W. N. Speckamp, and H. O. Huisman, *ibid.*, 1970, 2527.

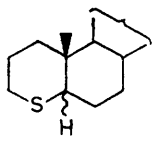
[5] H. O. Huisman in 'Steroids,' ed. W. F. Johns, MTP International Review of Science, Butterworths University Park Press, London, 1973, p. 240.

[6] P. Laur, H. Hauser, J. E. Gurst, and K. Mislow, *J. Org. Chem.*, 1967, **32**, 498; G. Lehmann, H. Schick, B. Lucke, and G. Hilgetag, *Ber.*, 1968, **101**, 787; M. Kishi and T. Komeno, *Tetrahedron*, 1971, **27**, 1527; M. E. Wolff and G. Zanati, *Experientia*, 1970, **26**, 1115; *J. Medicin. Chem.*, 1970, **13**, 563; 1969, **12**, 629; M. E. Wolff, G. Zanati, G. Shanmugasundarum, S. Gupte, and G. Aadahl, *ibid.*, p. 531.

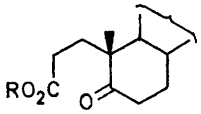
[7] For references to recent examples see D. N. Jones in 'Organic Compounds of Sulphur, Selenium, and Tellurium,' Chem. Soc. Specialist Periodical Report, 1972, p. 135.

[8] J. T. Edward and P. F. Morand, *Canad. J. Chem.*, 1960, **38**, 1325.

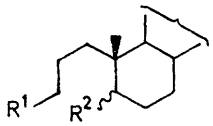
isopropoxide in hot toluene gave a complex mixture of products which did not contain 4-thia-5α- or 5β-cholestane, according to t.l.c. comparison with samples obtained subsequently. Under these conditions the displacement of sulphonate ester groups by thiolate



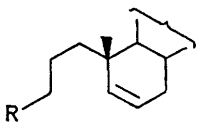
(I) 5β-H
(II) 5α-H



(III) R = H
(XIII) R = Me



	R^1	R^2
(IV)	OH	5α-OH
(V)	OH	5β-OH
(VI)	O·SO_2Me	5α-O·SO_2Me
(VII)	O·SO_2Me	5β-O·SO_2Me
(VIII)	S·COMe	5α-O·SO_2Me
(IX)	S·COMe	5β-O·SO_2Me
(X)	SH	5β-O·SO_2Me



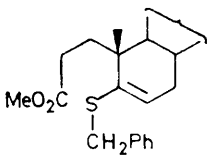
	R
(XI)	S·COMe
(XII)	SH
(XV)	CO_2Me
(XVI)	OH
(XVII)	OH (5,6-dihydro)
(XVIII)	O·SO_2Me
(XIX)	SCN
(XXXI)	SOH
(XXXII)	SBu^t
(XXXIII)	S(O)Bu^t

anions usually occurs readily.[9] We attribute the virtual absence of intramolecular displacement of the 5-methanesulphonate group by the 3-thiolate anion to steric retardation caused by the tertiary centre at C-10, and the formation of many products to skeletal (Wagner–Meerwein) rearrangements of the carbocation formed by solvolysis of the 5-methanesulphonate. There is analogy for such behaviour in the reactions of neopentyl halides,[10] and in the rearrangements of 5-substituted cholestanes.[11] We expected some complications from the start, but we investigated this method of constructing thian rings initially because it had been successful in other systems incorporating leaving groups at neopentyl centres,[2a,12] and because the diols (IV) and (V) were readily available. That rearrangements accompany solvolysis in these systems was indicated by the behaviour of the thioacetoxy-methanesulphonates (VIII) and (IX) in hot aqueous acidic ethanol. Five products were obtained, according to t.l.c. on silica impregnated with silver nitrate, a medium useful for separating isomeric olefins;[13] the products had identical chromatographic mobilities (t.l.c.) on silica alone. Spectroscopic data indicated the presence of a thioacetoxy-group ($\nu_{max.}$ 1790 cm^{-1}, τ 7·71) and vinyl protons (τ 5·36, 5·22, and 4·97) and the combustion analytical data were those expected for 3-acetylthio-A-nor-3,5-secocholest-5-ene (XI), but direct comparison of the n.m.r. spectrum of the mixture with that of an authentic specimen of (XI) (prepared subsequently) showed that this compound was absent. The products were therefore isomeric unsaturated thioacetates, formed by rearrangements following the heterolysis of the 5-methanesulphonate groups, but their structures were not investigated further.

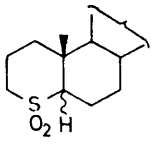
We next investigated a synthetic route involving the intramolecular addition of a thio-radical, produced photochemically from the 3-thiol, to the 5,6-double bond in A-nor-3,5-secocholest-5-ene-3-thiol (XII). Such intramolecular free radical additions, which had precedent,[14] were expected to proceed without molecular rearrangement.[15] The introduction of the 5,6-double bond was achieved in a manner designed to avoid the rearrangements which accompanied the formation of an incipient carbocation at C-5. Methyl 5-oxo-A-nor-3,5-secocholestan-3-oate (XIII) reacted with toluene-α-thiol in boiling benzene containing molecular sieves to give methyl 5-benzylthio-A-nor-3,5-secocholest-5-en-3-oate (XIV), which on treatment with Raney nickel in boiling acetone[16] gave methyl A-nor-3,5-secocholest-5-en-3-oate (XV). A similar method for the conversion of ketones into olefins which precludes molecular rearrangements has been described recently.[17] Reduction of the ester (XV) with lithium aluminium hydride gave the unsaturated alcohol (XVI), which was reduced further by hydrogen over platinum to A-nor-3,5-secocholestan-3-ol (XVII). The alcohol (XVII) was also obtained when the enethiol ether (XIV) was treated in sequence with Raney nickel in ethanol (during which hydrogenolysis of the enethiol ether was accompanied by reduction of the double bond) and lithium aluminium hydride. The methanesulphonate (XVIII), derived from the alcohol (XVI) and methanesulphonyl chloride, reacted with tetrabutylammonium thioacetate in acetone, or with potassium thioacetate generated *in situ* in acetonitrile,[18] to give 3-acetylthio-A-nor-3,5-secocholest-5-ene (XI), and with potassium thiocyanate in acetone the methanesulphonate (XVIII) gave the thiocyanate (XIX). Reduction of the thioacetate (XI) and the thiocyanate (XIX) with lithium aluminium hydride gave A-nor-3,5-secocholest-5-ene-3-thiol (XII). Irradiation of a solution of the unsaturated thiol (XII) in cyclohexane with

[9] D. N. Jones, D. Mundy, and R. D. Whitehouse, *J. Chem. Soc.* (*C*), 1969, 1668.
[10] I. Dostrovsky and E. D. Hughes, *J. Chem. Soc.*, 1946, 157, 161, 164, 166, 169, 171; I. Dostrovsky, E. D. Hughes, and C. K. Ingold, *ibid.*, p. 173.
[11] D. N. Kirk and M. P. Hartshorn, 'Steroid Reaction Mechanisms,' Elsevier, London, 1968, p. 257.
[12] L. A. Paquette and J. C. Philips, *J. Amer. Chem. Soc.*, 1968, **90**, 3898; *Chem. Comm.*, 1969, 680; R. M. Dodson, P. J. Cahill, and B. H. Chollar, *ibid.*, p. 310.
[13] L. J. Morris, *Chem. and Ind.*, 1962, 1238.
[14] J. M. Surzur, M. P. Crozet, and C. Dupuy, *Tetrahedron Letters*, 1971, 2025; J. M. Surzur, R. Nouguier, M. P. Crozet, and C. Dupuy, *ibid.*, p. 2035.
[15] C. Walling in 'Molecular Rearrangements,' ed. P. de Mayo, Interscience, New York, 1963, p. 407; C. Walling and A. Cioffari, *J. Amer. Chem. Soc.*, 1972, **94**, 6064.
[16] G. B. Spero, A. V. McIntosh, and R. H. Levin, *J. Amer. Chem. Soc.*, 1948, **70**, 1907.
[17] R. B. Boar, D. W. Hawkins, J. F. McGhie, and D. H. R. Barton, *J.C.S. Perkin I*, 1973, 654.
[18] P. S. Portoghese and V. G. Telang, *Tetrahedron*, 1971, **27**, 1823.

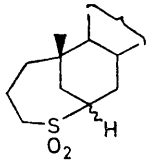
u.v. light gave 4-thia-5β-cholestane (I) (76%), in 36% overall yield from cholesterol. In assigning the structure (I) to the photoproduct we considered that addition of



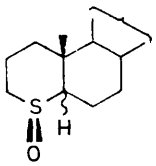
(XIV)



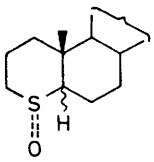
(XX) 5β-H
(XXI) 5α-H



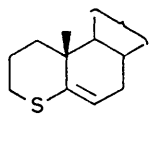
(XXII) 6β-H
(XXIII) 6α-H



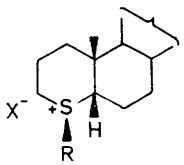
(XXIV) 5β-H
(XXVIII) 5α-H



(XXV) 5β-H
(XXIX) 5α-H



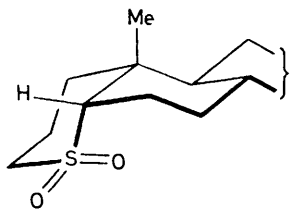
(XXVI)



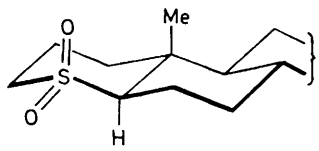
(XXVII) R = Cl, X = Bu^{t}O
(XXX) R = OEt, X = BF_4

the thio-radical to the double bond would occur preferentially at C-5 and not at C-6, because irradiation of hex-5-ene-1-thiol under comparable conditions gave predominantly 2-methylthian, with thiepan as a minor product.[14] The allocation of 5β-configuration followed from the known propensity of thio-radicals to react with cyclohexene derivatives to give predominantly axial sulphides.[19] These structural assignments were substantiated in the following manner. Oxidation of the steroidal thian (I) with 3-chloroperbenzoic acid gave the sulphone (XX), which was transformed into the isomeric sulphone (XXI) on treatment with potassium t-butoxide in benzene containing dicyclohexyl-18-crown-6.[20] This base-catalysed isomerisation, which finds analogy in the isomerisation of 5β-cholestan-4-one to 5α-cholestan-4-one,[21] is rational in terms of the transformation of a *cis*-fused AB ring system (*A*) into the thermodynamically more stable *trans*-fused AB ring system (*B*). Recently the base-catalysed isomerisation of other *cis*-1-thiadecalin 1,1-dioxide derivatives into their *trans*-isomers has been reported.[22] The isomerisation of the sulphone derived from the photoproduct also indicated that it was not the thiepan dioxide derivative (XXII); the isomeric structure (XXIII) was excluded because it is so strained that a Dreiding model of it cannot be constructed.

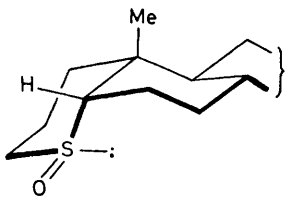
Oxidation of 4-thia-5β-cholestane (I) with peroxydodecanoic acid in light petroleum gave 4-thia-5β-cholestane 4β-oxide (XXIV) (93%) and 4-thia-5β-cholestane 4α-oxide (XXV) (2%), whereas oxidation of (I) with t-butyl hypochlorite in tetrahydrofuran–methanol gave a mixture of the oxides (XXIV) (27%) and (XXV) (44%), together with 4-thiacholest-5-ene (XXVI) (10%). The compound (XXVI) presumably arose by formal elimination of hydrogen chloride and a proton from the intermediate chlorosulphonium ion (XXVII) formed in such oxidations.[23] Configurations at sulphur were allocated on the basis of the known tendency of thians to be oxidised predominantly to equatorial thian oxides by peroxy-acids,[2b,24] and predominantly to axial thian oxides by t-butyl hypochlorite.[24] In accord with these assignments, (XXIV) (*C*) was chromatographically less mobile than (XXV) (*E*); it has been established for diastereoisomeric oxides of cyclic sulphides that the isomer with the sterically



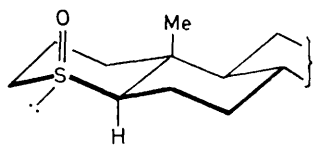
(*A*)



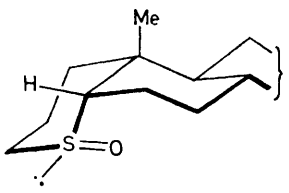
(*B*)



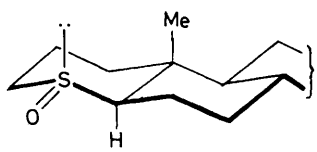
(*C*)



(*D*)



(*E*)



(*F*)

more accessible oxygen (usually the equatorial oxide) has the smaller R_F value.[2,24,25] Oxidation of the oxides

[19] E. S. Huyser and J. R. Jeffrey, *Tetrahedron*, 1965, **21**, 3083; E. S. Huyser, H. Benson, and H. J. Sinnige, *J. Org. Chem.*, 1967, **32**, 622.

[20] C. J. Pederson, *J. Amer. Chem. Soc.*, 1967, **89**, 7017; C. J. Pederson and H. K. Frensdorff, *Angew. Chem. Int. Edn.*, 1972, **11**, 16.

[21] N. L. Allinger, M. A. DaRooge, and R. B. Hermann, *J. Org. Chem.*, 1961, **26**, 3626.

[22] J. Kattenberg, E. R. de Waard, and H. O. Huisman, *Tetrahedron*, 1974, **30**, 463.

[23] C. R. Johnson and J. J. Rigau, *J. Amer. Chem. Soc.*, 1969, **91**, 5398.

[24] C. R. Johnson and D. McCants, *J. Amer. Chem. Soc.*, 1965, **87**, 1109.

[25] (*a*) J. J. Rigau, C. C. Bacon, and C. R. Johnson, *J. Org. Chem.*, 1970, **35**, 3655; (*b*) M. Kishi and T. Komeno, *Tetrahedron Letters*, 1971, 2641; (*c*) C. R. Johnson, H. Diefenbach, S. E. Keiser, and J. C. Sharp, *Tetrahedron*, 1969, **25**, 5649.

(XXIV) and (XXV) with 3-chloroperbenzoic acid gave the sulphone (XX), confirming that the oxides differed only in configuration at sulphur.

Treatment of 4-thia-5β-cholestane 4β-oxide (XXIV), in which oxygen is equatorial (*C*), with potassium t-butoxide in benzene containing dicyclohexyl-18-crown-6 gave an equilibrium mixture of (XXIV) and 4-thia-5α-cholestane 4β-oxide (XXVIII), in which oxygen is axial (*D*). The ratio of (XXIV) to (XXVIII) was *ca.* 56 : 44 at 80°, corresponding to a standard free-energy difference of *ca.* 140 cal mol^{-1} between the isomers. Since the *syn*-axial repulsive interaction between sulphinyl oxygen and a methyl group in 3,3-dimethylthian 1-oxide has been estimated to exceed 2 kcal mol^{-1},[26] the result of the equilibration of (XXIV) and (XXVIII) suggests that 4-thia-5β-cholestane (I) is less thermodynamically stable than its 5α-isomer (II) by at least 1·86 kcal mol^{-1}. Under the same basic conditions 4-thia-5β-cholestane 4α-oxide (XXV), in which the oxygen is axial (*E*), was converted quantitatively into 4-thia-5α-cholestane 4α-oxide (XXIX), in which the oxygen is equatorial (*F*). This isomerisation is rational in terms of the greater thermodynamic stability of the *trans*- than the *cis*-fused AB ring system, augmented by the known preference of sulphinyl oxygen in 3,3-dialkylthian 1-oxide systems for the equatorial orientation.[26] As expected,[2,24,25] the axial sulphoxide (XXVIII) (*D*) displayed a larger R_F value on silica (t.l.c.) than the equatorial sulphoxide (XXIX) (*F*).

4-Thia-5α-cholestane 4β-oxide (XXVIII) was reduced to 4-thia-5α-cholestane (II) by phosphorus trichloride in boiling methylene chloride,[27] and oxidation of the steroidal thian (II) with peroxydodecanoic acid in light petroleum gave the equatorial sulphoxide (XXIX) exclusively, in accord with the known behaviour of peroxy-acids with cyclic sulphides.[2b,24]

The oxidation of 4-thia-5β-cholestane (I) to the oxides (XXIV) and (XXV) by t-butyl hypochlorite was capricious, so that 4-thia-5β-cholestane 4α-oxide (XXV) was the least conveniently available of the steroidal thian oxides. The use of oxidants such as *N*-chlorobenzotriazole,[28] ozone, and hydrogen peroxide with 4-thia-5β-cholestane gave smaller yields of the 4α-oxide (XXV) (relative to the 4β-oxide) confirming the indications of other investigations[24,25] that t-butyl hypochlorite, albeit capricious in our hands, was the oxidant of choice for converting (I) into (XXV). Since appreciable quantities of the 4α-oxide (XXV) were required for other studies we investigated other methods of making it. Attempted inversion of configuration at sulphur in the readily available 4β-oxide (XXIV) by Johnson's method[29] was unsuccessful; the sulphoxide (XXIV) gave the ethoxysulphonium salt (XXX) with triethyloxonium tetrafluoroborate, but hydrolysis of the salt gave only starting sulphoxide (XXIV). Evidently displacement of the ethoxy-group by rear attack of hydroxide ions at sulphur did not occur, which is reasonable according to models because the rear face of the sulphur atom is encompassed by the fold of the *cis*-fused AB ring system [*cf.* (*C*)] and is therefore sterically hindered. The starting sulphoxide was regenerated probably by nucleophilic attack of hydroxide ion at carbon with fission of the C–O bond. On treatment with hydrochloric acid in dioxan,[30] conditions which usually cause equilibration at sulphur in sulphoxides,[2b,24,25a,30] 4-thia-5β-cholestane 4β-oxide (XXIV) remained unchanged. This was not unexpected, since analogy with the conformational preference of 3,3-dimethylthian 1-oxide[26] suggested that the axial 4α-sulphoxide (XXV) (*E*) should be considerably less stable thermodynamically than the equatorial 4β-sulphoxide (XXIV) (*C*). However it was surprising that 4-thia-5α-cholestane 4β-oxide (XXVIII), in which oxygen is *syn*-axial to the 10-methyl group (*D*), was also inert under these conditions; Kishi and Komeno[25b] also failed to equilibrate diastereoisomeric sulphoxides with hydrochloric acid in dioxan.

TABLE 1

Photocatalysed stereomutation of the 4-thiacholestane 4-oxides

Compound irradiated	Steady-state composition of product mixture (%) (XXIV)	(XXV)	(XXVIII)	(XXIX)	Recovery (%)	Irradiation * time (h)
(XXIV)	61	39			79	4
(XXV)	29	71			79	5
(XXVIII)			54	46	70	3
(XXIX)			25	75	82	5

* Time after which the relative proportions of the sulphoxides in the product mixture remained unaltered.

These observations led to an investigation of the thermal and photochemical stability of the steroidal sulphoxides (XXIV), (XXV), (XXVIII), and (XXIX). They were configurationally stable in boiling decalin, in contrast to the behaviour of other thian 1-oxides under these conditions.[24,31] However, on irradiation at 254 nm in ether solution the sulphoxides underwent stereomutation at sulphur (Table 1). Irradiation was continued until the ratio of sulphoxides was constant, according to t.l.c. Prolonged irradiation caused decomposition, and true equilibrium mixtures were not obtained. Photoinduced stereomutation at sulphur, an

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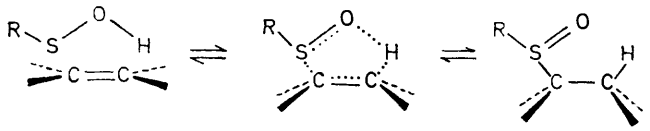
established phenomenon for diaryl and aryl alkyl sulphoxides,[32] has only recently been encountered in dialkyl sulphoxides,[25b,33] and in these cases a mechanism involving simple pyramidal inversion was considered unlikely. The photoinduced stereomutation of penicillin sulphoxides apparently involved homolysis and reformation of a carbon–sulphur bond with loss of stereochemical integrity in the intermediate diradicals,[34] but it appears that this does not apply for the photocatalysed stereomutation at sulphur in the sulphoxides (XXIV), (XXV), (XXVIII), and (XXIX) since there is no concomitant stereomutation at C-5; we consider it unlikely that homolysis of the C(5)–S bond would be attended by retention of stereochemical integrity of a C-5 radical whilst the sulphinyl radical loses its stereochemical identity, and equally unlikely that homolysis–recombination occurs only in the C(3)–S bond. The evidence points to photocatalysed inversion at sulphur, but this conclusion must be regarded as tentative in view of the partial decomposition and the failure to generate equilibrium mixtures.

We devised a more direct stereospecific synthesis of 4-thia-5β-cholestane 4α-oxide (XXV) which exploited the stereoelectronic requirements of the addition of sulphenic acids to olefins.[35] This addition is one facet of a reversible six-electron sigmatropic rearrangement,[36] the other being the pyrolytic elimination of a sulphoxide to give an olefin and a sulphenic acid, for which a concerted *syn*-intramolecular mechanism has been established (Scheme).[37] In the transition state (*G*) the



(*G*)

SCHEME

five participating atoms tend towards coplanarity,[38] and models show that for the intramolecular addition of the sulphenic acid to the double bond in (XXXI) a transition state with the required geometry is possible only when addition leads to 4-thia-5β-cholestane 4α-oxide (XXV). The sulphenic acid (XXXI) was generated in the following manner. Treatment of the unsaturated methanesulphonate (XVIII) with thio-t-butoxide ions in propan-2-ol gave the t-butyl sulphide (XXXII), which on oxidation with peroxydodecanoic acid gave the sulphoxide (XXXIII). Pyrolysis of the sulphoxide (XXXIII) in boiling xylene gave 4-thia-5β-cholestane 4α-oxide (XXV) (48%) and no trace of the isomeric steroidal thian oxides, indicating that the t-butyl sulphoxide (XXXIII) had decomposed to the sulphenic acid (XXXI), which had in turn cyclised in the expected manner to give the 4α-oxide (XXV). The thermal decomposition of the sulphoxide (XXXIII) to the sulphenic acid (XXXI) finds analogy in the thermolysis of di-t-butyl sulphoxide to give the very reactive 2-methylpropane-2-sulphenic acid.[39] If the regioselectivity of elimination of the sulphoxide (XXXIII) is governed by statistical factors related to the number of available β-hydrogen atoms,[40] the cyclisation of (XXXI) to (XXV) must have occurred in *ca.* 59% yield. This stereospecific synthesis, together with the transformations described earlier, confirmed the structures allocated to all the steroidal thian oxides.

The n.m.r. characteristics of the steroidal thian oxides (Table 2) were in accord with the allocated structures. The 10-methyl proton signal of 4-thia-5α-cholestane 4β-oxide (XXVIII) (*D*) occurred 28 Hz downfield of its position in the spectrum of 4-thia-5α-cholestane (II) as a consequence of the '*syn*-axial effect' of the sulphinyl

TABLE 2

N.m.r. data (τ values) for 4-thiacholestanes and their oxides and dioxides

Compound	Solvent	13-Me	10-Me
(I)	$CDCl_3$	9·34	9·01
	C_6D_6	9·40	9·10
(II)	$CDCl_3$	9·35	8·95
	C_6D_6	9·36	8·89
(XXIV)	$CDCl_3$	9·34	8·92
	C_6D_6	9·45	9·32
(XXV)	$CDCl_3$	9·35	8·99
	C_6D_6	9·36	9·30
(XXVIII)	$CDCl_3$	9·33	8·67
	C_6D_6	9·42	8·61
(XXIX)	$CDCl_3$	9·34	9·04
	C_6D_6	9·42	9·31
(XX)	$CDCl_3$	9·34	8·93
(XXI)	$CDCl_3$	9·34	8·82

oxygen,[2b,41] whereas in 4-thia-5α-cholestane 4α-oxide (XXIX) (*F*) an upfield shift of 9 Hz was observed. The apparent shielding of the 10-methyl group by the axial lone electron pair in (XXIX) (*F*) finds analogy in the n.m.r. behaviour of the 10-methyl group in 2-thia-5α-androstan-17β-ol 2α-oxide,[2b] and may be compared with the shielding of protons by a '*syn*-axial' lone electron pair on sulphinyl sulphur in derivatives of thian

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1-oxide,[42] thiolan 1-oxide,[25b,43] thietan 1-oxide,[44] and 2-thia-5-azabicyclo[2.2.1]heptane 2-oxide.[18] The shifts in the 10-methyl group signals on changing solvent from deuteriochloroform to deuteriobenzene were in accord with the prediction, based on Ledaal's model,[41] that protons on the side of the molecule opposite to that of sulphinyl oxygen should become more shielded relative to those on the same side; the shifts were 27 Hz upfield for (XXIX) (*F*) and 6 Hz downfield for (XXVIII) (*D*). Overlapping of signals precluded an analysis of the n.m.r. characteristics of the protons adjacent to the sulphinyl group, which in suitable cases has provided information about the conformation and configuration of cyclic sulphoxides.[26,43]

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. I.r. spectra were determined for solutions in chloroform with a Unicam SP 100 spectrophotometer, and n.m.r. spectra with a Varian HA-100 spectrometer for solutions in deuteriochloroform. Optical rotations were determined with a Perkin-Elmer 141 automatic polarimeter for solutions in chloroform. Preparative thick-layer chromatography (p.l.c.) was performed with a 1 mm layer of silica gel G (Merck). Light petroleum refers to the fraction b.p. 40—60°.

A-*Nor*-3,5-*secocholestane* 3,5α-*diol* (IV) *and its* 5β-*Epimer* (V).—5-Oxo-A-nor-3,5-secocholestan-3-oic acid[45] (III) (5·0 g) was treated with lithium aluminium hydride (1·4 g) in ether overnight at room temperature. After careful dropwise addition of water the solution was worked up in the usual manner to give a solid residue (4·53 g) which was chromatographed on a column of silica gel (250 g) eluted with ether–benzene (3 : 2). The 3,5α-diol (IV) (0·9 g, 19%), m.p. 129—131° (from methanol), $[\alpha]_D$ +46° (*c* 1·1) (lit.,[8] m.p. 130—131°, $[\alpha]_D$ +46°) was eluted first, followed by a mixture of (IV) and (V) (0·5 g, 10%) and then the 3,5β-diol (V) (3·02 g, 63%), m.p. 133—135° (from methanol), $[\alpha]_D$ +24° (*c* 0·6) (lit.,[8] m.p. 134—135°, $[\alpha]_D$ +25°).

3,5α-*Bismethylsulphonyloxy*-A-*nor*-3,5-*secocholestane* (VI) *and its* 5β-*Epimer* (VII).—(*a*) The 3,5α-diol (IV) (300 mg) in dry pyridine (8·5 ml) was treated with methanesulphonyl chloride (1 ml) at 0° overnight. The mixture was poured into ice-cold 2N-hydrochloric acid and extracted with ether, and the extract was washed and dried in the usual way to give the 3,5α-*bismethanesulphonate* (VI) (345 mg, 82%), m.p. 100—101° (needles from ether–methanol), $[\alpha]_D$ +42° (*c* 0·2), τ 9·33 (3H, s, 13-Me), 9·12 (3H, s, 10-Me), 7·03 (3H, s, SO_2Me), 7·00 (3H, s, SO_2Me), 5·81 (2H, m, $CH_2{\cdot}SO_2$), and 5·30 (1H, $W_{\frac{1}{2}}$ 8 Hz, 5β-H) (Found: C, 61·6; H, 9·7; S, 12·0. $C_{28}H_{52}O_6S_2$ requires C, 61·3; H, 9·6; S, 11·7%).

(*b*) The 3,5β-diol (V) (1·5 g) in dry pyridine (51 ml) was treated with methanesulphonyl chloride (5·7 ml) at 0° overnight. Work-up as before gave the 3,5β-*bismethanesulphonate* (VII) (1·67 g, 80%), m.p. 95—97° (needles from ether–methanol), $[\alpha]_D$ +10° (*c* 0·9), τ 9·35 (3H, s, 13-Me), 9·08 (3H, s, 10-Me), 7·03 (3H, s, SO_2Me), 7·01 (3H, s, SO_2Me), 5·81 (2H, m, $CH_2{\cdot}SO_2$), and 5·20 (1H, dd, $J_{5.6ax}$ 10, $J_{5.6eq}$ 5 Hz, 5α-H) (Found: C, 61·1; H, 9·4; S, 11·6%).

3-*Acetylthio*-5α-*methylsulphonyloxy*-A-*nor*-3,5-*secocholestane* (VIII) *and its* 5β-*Epimer* (IX).—(*a*) Tetrabutylammonium thioacetate (399 mg) was added to the 3,5α-bismethanesulphonate (VI) (65 mg) in boiling dry acetone (30 ml) under reflux. After 2 h the acetone was removed under reduced pressure and the residue was worked up with ether to give the 3-*thioacetate* 5α-*methanesulphonate* (VIII) (63 mg, 99%) as an oil, $[\alpha]_D$ +42° (*c* 0·2), $\nu_{max.}$ 1790, 1330, and 1165 cm^{-1}, τ 9·34 (3H, s, 13-Me), 9·11 (3H, s, 10-Me), 7·71 (3H, s, SAc), 7·18 (2H, m, $CH_2{\cdot}SO_2$), 6·98 (3H, s, SO_2Me), and 5·36 (1H, $W_{\frac{1}{2}}$ 7 Hz, 5β-H) (Found: C, 65·6; H, 9·7; S, 12·4. $C_{29}H_{52}O_4S_2$ requires C, 65·9; H, 9·9; S, 12·2%).

(*b*) The 3,5β-bismethanesulphonate (IX) (860 mg) was treated with tetrabutylammonium thioacetate (1·3 g) in boiling dry acetone (500 ml) for 20 min. The solvent was removed under reduced pressure and the residue was worked up with ether to give a brown oil which was chromatographed (p.l.c.) with benzene–ether (9 : 1) as eluant. Extraction of the major band provided the 3-*thioacetate* 5β-*methanesulphonate* (IX) (541 mg, 65%) as an oil, $[\alpha]_D$ +8° (*c* 1·5), $\nu_{max.}$ 1790, 1330, and 1165 cm^{-1}, τ 9·36 (3H, s, 13-Me), 9·11 (3H, s, 10-Me), 7·71 (3H, s, SAc), 7·19 (2H, m, $CH_2{\cdot}SO_2$), 7·00 (3H, s, SO_2Me), and 5·46 (1H, dd, $J_{5.6ax}$ 11, $J_{5.6eq}$ 5 Hz, 5α-H) (Found: C, 66·1; H, 9·9; S, 12·1%).

Treatment of the 3-*Thioacetate* 5β-*Methanesulphonate* (IX) *and its* 5α-*Isomer* (VIII) *with Acidic Ethanol*.—The 3-thioacetate 5β-methanesulphonate (IX) (1·5 g) was treated with a boiling mixture of 95% ethanol (120 ml) and 2N-hydrochloric acid (40 ml) for 1 h. After cooling, the solution was evaporated under reduced pressure to small bulk, and the residue was worked up with ether to give an oil, which was chromatographed (p.l.c.) with benzene–light petroleum (1 : 9) as eluant. Extraction of the band at R_F 0·5 gave an oil (550 mg), $\nu_{max.}$ 1790 cm^{-1} (SAc), τ 9·40 (s), 9·11 (s), 7·71 (s, SAc), 5·36, 5·22, and 4·97 (Found: C, 77·6; H, 11·0; S, 7·6. Calc. for $C_{28}H_{48}OS$: C, 77·7; H, 11·2; S, 7·4%). The oil gave one discrete spot on silica (t.l.c.) with benzene–light petroleum (1 : 9) as eluant, but on t.l.c. on silica impregnated with silver nitrate[13] with benzene as eluant five prominent spots and other minor spots were obtained. Treatment of the 5α-isomer (VIII) in the above manner gave a similar product mixture, according to t.l.c.

Methyl 5-*Benzylthio*-A-*nor*-3,5-*secocholest*-5-*en*-3-*oate* (XIV).—A solution of methyl 5-oxo-A-nor-3,5-secocholestan-3-oate[46] (XIII) (23·9 g), toluene-α-thiol (12·5 ml), and toluene-*p*-sulphonic acid (1·25 g) in dry benzene (240 ml) was boiled under reflux in a Soxhlet apparatus, with molecular sieves (4A; 150 g) in the thimble. After 48 h the solution was poured into 5% sodium carbonate solution and extracted with ether; the extracts were worked up to give the *product* (XIV) (28 g, 93%) as an oil, $[\alpha]_D$ −9° (*c* 0·5), τ 9·35 (3H, s, 13-Me), 8·98 (3H, s, 10-Me), 6·39 (3H, s, CO_2Me), 6·17 (2H,s, $S{\cdot}CH_2$), 4·47 (1H, d, *J* 5 Hz, 6-H), and 2·75 (5H, Ph) (Found: C, 77·5; H, 10·2; S, 6·2. $C_{34}H_{52}O_2S$ requires C, 77·8; H, 10·0; S, 6·1%).

Methyl A-*Nor*-3,5-*secocholest*-5-*en*-3-*oate* (XV).—Freshly prepared W-2 Raney nickel[47] (600 g) was stirred in boiling dry acetone (2·5 l) under reflux for 1 h, and a solution of the benzyl thioether (XIV) (27 g) in dry acetone (500 ml)

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was added in one portion. After boiling for a further 14 h the nickel was removed by filtration through Hiflo Supercel, and the filtrate was evaporated to give the *ester* (XV) (18·8 g, 91%) as an oil, $[\alpha]_D$ 0° (*c* 2·2), τ 9·31 (3H, s, 13-Me), 9·10 (3H, s, 10-Me), 6·38 (3H, s, CO_2Me), and 4·76 and 4·42 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 80·4; H, 11·6. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·5%).

A-*Nor*-3,5-*secocholest*-5-*en*-3-*ol* (XVI).—Lithium aluminium hydride (2 g) was added to the ester (XV) (6·6 g) in dry ether (150 ml), and after 1 h at room temperature the solution was worked up to give the *product* (XVI) (5·53 g, 91%) as an oil, $[\alpha]_D$ −10° (*c* 0·8), τ 9·33 (3H, s, 13-Me), 9·11 (3H, s, 10-Me), 6·45 (2H, m, CH_2·O), 4·715 and 4·445 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 83·1; H, 12·4. $C_{26}H_{46}O$ requires C, 83·4; H, 12·4%).

A-*Nor*-3,5-*secocholestan*-3-*ol* (XVII).—(*a*) The 5-en-3-ol (XVI) (600 mg) in ethyl acetate containing 65% perchloric acid (3 drops) was hydrogenated over platinum generated from platinum oxide (25 mg). After 3 h, uptake was complete, and the platinum was removed by filtration through Hiflo Supercel. Evaporation gave the 3-*ol* (XVII) (520 mg, 86%), m.p. 73—74° (from acetone–methanol), $[\alpha]_D$ +26° (*c* 0·8), τ 9·35 (3H, s, 13-Me), 9·12 (3H, s, 10-Me), and 6·46 (2H, m, CH_2·O) (Found: C, 82·8; H, 12·6. $C_{26}H_{48}O$ requires C, 82·9; H, 12·9%).

(*b*) The benzyl thioether (XIV) (20 mg) was treated with W-2 Raney nickel [47] (200 mg) in boiling ethanol for 4 h. Removal of the nickel and evaporation of the filtrate gave an oil (15 mg) which was treated with lithium aluminium hydride (20 mg) in ether (5 ml) at room temperature for 16 h. The usual work-up gave the 3-ol (XVII) (11 mg, 77%), identical with the sample described in (*a*).

3-*Methylsulphonyloxy*-A-*nor*-3,5-*secocholest*-5-*ene* (XVIII).—Methanesulphonyl chloride (50 ml) was added to the 3-ol (XVI) (9·8 g) in pyridine (280 ml) at 0°, and the mixture was allowed to warm to room temperature. After 2 h the usual work-up gave the *product* (XVIII) (11·8 g, 99%) as an oil, $[\alpha]_D$ −5° (*c* 1·0), τ 9·32 (3H, s, 13-Me), 9·10 (3H, s, 10-Me), 6·94 (3H, s, $MeSO_2$), 5·86 (2H, m, CH_2·SO_2), and 4·74 and 4·435 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 71·4; H, 10·5; S, 7·2. $C_{27}H_{48}O_3S$ requires C, 71·6; H, 10·7; S, 7·1%).

3-*Acetylthio*-A-*nor*-3,5-*secocholest*-5-*ene* (XI).—(*a*) Tetrabutylammonium thioacetate (6·75 g) was added to a solution of the 3-methanesulphonate (XVIII) (5 g) in dry acetone (420 ml) and the mixture was boiled under reflux for 2 h. The solvent was removed under reduced pressure and the residue was worked up with ether to give an oil which was chromatographed (p.l.c.) on silica with benzene–light petroleum (1 : 3) as eluant. Extraction of the major band gave the *product* (XI) (3·3 g, 70%) as an oil, $[\alpha]_D$ +10° (*c* 2·1), τ 9·33 (3H, s, 13-Me), 9·11 (3H, s, 10-Me), 7·70 (3H, s, Ac), 7·19 (2H, m, CH_2·S), and 4·73 and 4·445 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 77·9; H, 11·0; S, 7·6. $C_{28}H_{48}OS$ requires C, 77·7; H, 11·2; S, 7·4%).

(*b*) Anhydrous potassium carbonate (1·7 g) was added to a solution of the 3-methanesulphonate (XVIII) (850 mg) in acetonitrile (20 ml) and thioacetic acid (0·11 ml) in acetonitrile (10 ml) was added dropwise to the boiling mixture. After addition was complete boiling was continued for 1 h and the solvent was removed under reduced pressure. Extraction of the residue with ether and the usual work-up gave the 3-thioacetate (0·71 g, 87%), identical with the product described in (*a*).

3-*Thiocyanato*-A-*nor*-3,5-*secocholest*-5-*ene* (XIX).—Potassium thiocyanate (25 g) was added to a solution of the 3-methanesulphonate (XVIII) (11·8 g) in dry acetone (600 ml), and after boiling for 6 h the acetone was removed under reduced pressure and the residue was extracted with light petroleum. After washing with water and drying, evaporation gave the *product* (XIX) (9·2 g, 85%) as an oil, $[\alpha]_D$ +10° (*c* 1·3), $\nu_{max.}$ 2155 cm^{-1} (SCN), τ 9·33 (3H, s, 13-Me), 9·10 (3H, s, 10-Me), 7·10 (2H, m, CH_2·SCN), and 4·72 and 4·395 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 77·9; H, 10·7; N, 3·3; S, 7·9. $C_{27}H_{45}NS$ requires C, 78·0; H, 10·9; N, 3·4; S, 7·7%).

A-*Nor*-3,5-*secocholest*-5-*ene*-3-*thiol* (XII).—(*a*) Lithium aluminium hydride (30 mg) was added to the 3-thioacetate (XI) (80 mg) in dry ether (20 ml), and after 30 min at room temperature the usual work-up gave the *product* (XII) (71 mg, 98%) as an oil, $[\alpha]_D$ 0° (*c* 0·5), τ 9·33 (3H, s, 13-Me), 9·11 (3H, s, 10-Me), 8·71 (1H, s, SH), 7·55 (2H, m, CH_2·S), and 4·72 and 4·445 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 79·7; H, 11·7; S, 8·3. $C_{26}H_{46}S$ requires C, 79·9; H, 11·9; S, 8·2%).

(*b*) The 3-thiocyanate (102 mg) in dry ether (20 ml) was treated with lithium aluminium hydride (40 mg) for 15 min at room temperature. The usual work-up gave the 3-thiol (90 mg, 94%), identical with the sample described in (*a*).

4-*Thia*-5β-*cholestane* (I).—A solution of the 3-thiol (XII) (320 mg) in hexane (17·5 ml; spectroscopic grade) was kept at room temperature under nitrogen in a water-cooled quartz vessel, and irradiated for 1·5 h with an Engelhard Hanovia Chromatoscope low-pressure u.v. lamp transmitting from 200 to 400 nm (max. 254 nm). The solvent was removed under reduced pressure and the residue was chromatographed (p.l.c.) on silica eluted with light petroleum. Extraction of the major band gave 4-*thia*-5β-*cholestane* (I) (244 mg, 76%), m.p. 99—101° (from ether–methanol), $[\alpha]_D$ −27° (*c* 0·4), τ 9·34 (3H, s, 13-Me), 9·02 (3H, s, 10-Me), 7·41 (2H, m, CH_2·S), and 7·08 (1H, dd, J_{AX} 4, J_{AY} 2·25 Hz, 5β-H) (Found: C, 80·0; H, 11·6; S, 8·2. $C_{26}H_{46}S$ requires C, 79·9; H, 11·9; S, 8·2%).

4-*Thia*-5β-*cholestane* 4β-*Oxide* (XXIV) *and* 4α-*Oxide* (XXV).—(*a*) Peroxydodecanoic acid (70% pure; 310 mg) was added to a solution of 4-thia-5β-cholestane (I) (414 mg) in light petroleum (50 ml), and after 30 min at room temperature the mixture was poured onto a column of neutral alumina. Elution with chloroform gave a mixture which was rechromatographed (p.l.c.) on silica eluted with ether–chloroform (2 : 1). Extraction of the band at R_F 0·2 gave the 4β-*oxide* (XXIV) (400 mg, 93%), m.p. 164—166° (from ether), $[\alpha]_D$ +81° (*c* 0·5), $\nu_{max.}$ 1018 cm^{-1}, τ 9·34 (3H, s, 13-Me), 8·92 (3H, s, 10-Me), and 6·56 (1H, d, *J* 12 Hz) (Found: C, 77·6; H, 11·3; S, 8·2. $C_{26}H_{46}OS$ requires C, 76·8; H, 11·4; S, 7·9%). Extraction of the band at R_F 0·6 gave the 4α-oxide (XXV) (8 mg, 2%), identical with a specimen obtained by oxidation of (I) with t-butyl hypochlorite.

(*b*) t-Butyl hypochlorite (34·4 mg) in dry methanol (0·25 ml) was added dropwise to a stirred solution of 4-thia-5β-cholestane (I) (124 mg) in dry tetrahydrofuran (6 ml) and methanol (1 ml) at −78°. After stirring at −78° for 1 h the temperature was allowed to rise to −40° and anhydrous sodium carbonate was added. Filtration and evaporation gave an oil which was chromatographed

(p.l.c.) on silica eluted with ether–chloroform (2 : 1). Extraction of the band at R_F 0·2 gave the 4β-oxide (XXIV) (35 mg, 27%), identical with the sample obtained earlier, and extraction of the band at R_F 0·6 gave the *4α-oxide* (XXV) (57 mg, 44%), m.p. 179—181° (from ether), $[\alpha]_D$ −49° (*c* 0·4), $\nu_{max.}$ 1016 cm^{-1}, τ 9·35 (3H, s, 13-Me), 8·99 (3H, s, 10-Me), and 7·02 (1H, m) (Found: C, 76·5; H, 11·2; S, 8·1%). A band at the solvent front was extracted and rechromatographed (p.l.c.) on silica eluted with light petroleum. Extraction of the band at R_F 0·4 gave starting material (I) (12 mg, 10%), and extraction of the band at R_F 0·5 gave *4-thiacholest-5-ene* (XXVI) (13 mg, 10%), m.p. 95—97° (from ether–methanol), $[\alpha]_D$ −118° (*c* 1·4), τ 9·32 (3H, s, 13-Me), 8·74 (3H, s, 10-Me), and 4·16 (1H, m, 6-H) (Found: *m/e* 388·3159. $C_{26}H_{46}S$ requires *m/e* 388·3164).

4-Thia-5α-cholestane 4β-Oxide (XXVIII).—A solution of 4-thia-5β-cholestane 4β-oxide (XXIV) (3·28 g), potassium t-butoxide (3·5 g), and dicyclohexyl-18-crown-6 (1·2 g) in dry degassed benzene (450 ml) was boiled under nitrogen for 24 h and poured into water. The mixture was extracted with ether and the extracts were washed and dried in the usual way to give a crystalline mixture which was chromatographed (p.l.c.) on silica eluted with ether–chloroform (2 : 1). Extraction of the band at R_F 0·2 gave starting material (XXIV) (1·8 g, 55%), and of the band at R_F 0·4 gave *4-thia-5α-cholestane 4β-oxide* (XVIII) (1·4 g, 43%), m.p. 183—185° (from acetone), $[\alpha]_D$ +85° (*c* 0·6), $\nu_{max.}$ 1040 cm^{-1}, τ 9·33 (3H, s, 13-Me), 8·67 (3H, s, 10-Me), and 6·95 (1H, d, *J* 12 Hz) (Found: C, 76·6; H, 11·2; S, 8·0. $C_{26}H_{46}OS$ requires C, 76·8; H, 11·4; S, 7·9%).

4-Thia-5α-cholestane (II).—A solution of 4-thia-5α-cholestane 4β-oxide (XXVIII) (568 mg) and phosphorus trichloride (0·62 ml) in methylene chloride (75 ml) was boiled for 30 min, poured into ice–water, and extracted with ether. After washing and drying evaporation of the extract gave *4-thia-5α-cholestane* (II) (540 mg, 99%), m.p. 110—112° (from ether–methanol), $[\alpha]_D$ +49° (*c* 0·6), τ 9·35 (3H, s, 13-Me) and 8·95 (3H, s, 10-Me) (Found: C, 79·8; H, 11·8; S, 8·2. $C_{26}H_{46}S$ requires C, 79·9; H, 11·9; S, 8·2%).

4-Thia-5α-cholestane 4α-Oxide (XXIX).—A solution of 4-thia-5α-cholestane (II) (128 mg) and peroxydodecanoic acid (92% pure; 77 mg) in light petroleum (10 ml) was kept at room temperature for 30 min and then poured onto a column of neutral alumina (4 g). Elution with light petroleum gave starting material (II) (18 mg, 14%) and elution with chloroform gave *4-thia-5α-cholestane 4α-oxide* (XXIX) (112 mg, 84%), m.p. 171—173° (from ether), $[\alpha]_D$ −29° (*c* 0·5), $\nu_{max.}$ 1024 cm^{-1}, τ 9·34 (3H, s, 13-Me), 9·04 (3H, s, 10-Me), and 6·55 (1H, d, *J* 11 Hz) (Found: C, 75·3; H, 11·25; S, 7·6; *m/e* 406·3268. $C_{26}H_{46}OS,0·5H_2O$ requires C, 75·1; H, 11·40; S, 7·7%. $C_{26}H_{46}OS$ requires *m/e* 406·3269).

(*b*) A solution of 4-thia-5β-cholestane 4α-oxide (XXV) (29 mg), potassium t-butoxide (30 mg), and dicyclohexyl-18-crown-6 (15 mg) in dry degassed benzene (5 ml) was boiled under nitrogen for 5 h, and then worked up in the usual way to give an oil which was chromatographed (p.l.c.) on silica eluted with ether–chloroform (2 : 1). Extraction of the major band gave 4-thia-5α-cholestane 4α-oxide (XXIX) (25 mg, 86%), identical with the sample prepared earlier. No starting material remained, according to t.l.c.

4-Thia-5β-cholestane 4,4-Dioxide (XX).—(*a*) A solution of 3-chloroperbenzoic acid (195 mg) and 4-thia-5β-cholestane (I) (150 mg) in ether (15 ml) was left overnight at temperature, and then worked up in the usual manr give the *product* (XX) (160 mg, 99%), m.p. 206—208° (from methanol), $[\alpha]_D$ +22° (*c* 1·1), $\nu_{max.}$ 1307, 1292, 1132, and 1111 cm^{-1}, τ 9·34 (3H, s, 13-Me) and 8·93 (3H, s, 10-Me) (Found: C, 74·1; H, 10·8; S, 7·8. $C_{26}H_{46}O_2S$ requires C, 73·9; H, 11·0; S, 7·6%). Oxidations of 4-thia-5β-cholestane 4β-oxide (XXIV) and 4-thia-5β-cholestane 4α-oxide (XXV) in the above manner gave the sulphone (XX) quantitatively.

4-Thia-5α-cholestane 4,4-Dioxide (XXI).—A solution of 4-thia-5β-cholestane 4,4-dioxide (XX) (122 mg), potassium t-butoxide (250 mg), and dicyclohexyl-18-crown-6 (61 mg) in dry degassed benzene (20 ml) was boiled overnight under nitrogen and worked up in the usual manner to give *4-thia-5α-cholestane 4,4-dioxide* (XXI) (115 mg, 96%), m.p. 203—205° (from ether), $[\alpha]_D$ +17° (*c* 0·7), $\nu_{max.}$ 1311, 1306, and 1131 cm^{-1}, τ 9·34 (3H, s, 13-Me) and 8·82 (3H, s, 10-Me) (Found: C, 73·6; H, 10·8; S, 7·8. $C_{26}H_{46}O_2S$ requires C, 73·9; H, 11·0; S, 7·6%).

(*b*) A solution of 4-thia-5α-cholestane (II) (200 mg) and 3-chloroperbenzoic acid (200 mg) in ether (20 ml) was left overnight at room temperature and then poured into saturated sodium hydrogen carbonate solution. The mixture was extracted with ether and the extract washed, dried, and evaporated to give the sulphone (XXI) (205 mg, 98%), identical with the sample prepared earlier. Oxidation of 4-thia-5α-cholestane 4β-oxide (XXVIII) and the 4α-oxide (XXIX) in the same way gave the sulphone (XXI) quantitatively.

3-t-Butylthio-A-nor-3,5-secocholest-5-ene (XXXII).—2-Methylpropane-2-thiol (4 ml) was added to a solution of sodium (1·1 g) in propan-2-ol (30 ml). After the addition of the 3-methanesulphonate (XVIII) (520 mg) in propan-2-ol (10 ml) the solution was boiled for 3 h, poured onto ice, and extracted with ether. The extract was washed, dried, and evaporated, and the residue was chromatographed on silica (p.l.c.) eluted with light petroleum. Extraction of the band at R_F 0·4 gave the *product* (XXXII) (0·41 g, 78%), m.p. 35—36°, $[\alpha]_D$ +9° (*c* 1·0), τ 9·33 (3H, s, 13-Me), 9·11 (3H, s, 10-Me), 8·70 (9H, s, Me_3C), 7·54 (2H, t, *J* 7 Hz, CH_2·S), and 4·44 and 4·70 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 80·65; H, 12·0; S, 7·3. $C_{30}H_{54}S$ requires C, 80·6; H, 12·2; S, 7·2%).

3-t-Butylsulphinyl-A-nor-3,5-secocholest-5-ene (XXXIII).—A solution of peroxydodecanoic acid (92% pure; 74 mg, 0·31 mmol) and the 3-t-butyl thioether (XXXII) (140 mg, 0·31 mmol) in light petroleum (11 ml) was kept at room temperature for 15 min and then poured onto a column of alumina (5 g) prepared in light petroleum. Elution with ether–chloroform (2 : 1) gave material which was chromatographed on silica (p.l.c.) eluted with ether–benzene (2 : 1). Extraction of the band at R_F 0·4 gave the *sulphoxide* (XXXIII) (110 mg, 76%), m.p. 98—101°, $[\alpha]_D$ +12° (*c* 0·6), $\nu_{max.}$ 1032 cm^{-1}, τ 9·30 (3H, s, 13-Me), 9·08 (3H, s, 10-Me), 8·76 (9H, s, Me_3C), 7·57 (2H, t, *J* 7 Hz, CH_2·S), and 4·40 and 4·68 (2H, AB part of an ABXY system, J_{AB} 10, J_{BX} 5, J_{BY} 0 Hz, 5- and 6-H) (Found: C, 77·6; H, 11·6; S, 7·0. $C_{30}H_{54}OS$ requires C, 77·85; H, 11·8; S, 6·9%).

Thermolysis of the Sulphoxide (XXXIII) *to give 4-Thia-5β-cholestane 4α-Oxide* (XXV).—The sulphoxide (XXXIII) (107 mg) in boiling xylene (100 ml) was kept for 5 h under nitrogen, and the solvent was then removed under reduced pressure. Chromatography of the residue on silica (p.l.c.)

with ether as eluant gave two bands at R_F 0·6 and 0·3, which were extracted to give, respectively, starting material (XXXIII) (2 mg) and 4-thia-5β-cholestane 4α-oxide (XXV) (45 mg, 48%), identical with the sample obtained earlier.

4β-*Ethoxy*-4-*thionia*-5β-*cholestane Tetrafluoroborate* (XXX).—Triethyloxonium tetrafluoroborate (21·7 mg) was added to 4-thia-5β-cholestane 4β-oxide (XXIV) (44·6 mg) in methylene chloride (2 ml), and the mixture was stirred for 30 min at room temperature. After cooling to 0°, addition of dry ether gave a white precipitate of the *product* (XXX) (31 mg, 54%), m.p. 198—199°, $[\alpha]_D$ +101° (*c* 0·7), τ 9·34 (3H, s, 13-Me), 8·79 (3H, s, 10-Me), 8·55 (3H, t, *J* 7 Hz, *Me*CH_2·O), 6·70 (1H, d, *J* 11 Hz), and 6·44 (2H, m) (Found: C, 64·1; H, 9·2. $C_{28}H_{51}F_4BOS$ requires C, 64·5; H, 9·7%).

The salt (XXX) (14 mg) in methanol (2 ml) containing water (0·1 ml) and sodium hydroxide (1·1 mg) was stirred at room temperature overnight and then boiled for 2 h. The usual work-up with ether gave 4-thia-5β-cholestane 4β-oxide (XXIV) (8·7 mg, 80%), identical with an authentic sample.

Stereomutation of the 4-*Thiacholestane* 4-*Oxides*.—A solution (0·01M) of each of the steroidal thian oxides in dry degassed ether was kept at room temperature under nitrogen in a water-cooled quartz vessel, and irradiated with an Engelhard Hanovia Chromatoscope low-pressure u.v. lamp transmitting from 200 to 400 nm (max. 254 nm). The reaction was monitored by t.l.c., and when the ratio of sulphoxides was constant the solvent was evaporated off, and the mixture of sulphoxides was separated from by-products by chromatography on silica (p.l.c.) eluted with ether–chloroform (2 : 1). Only stereomutation at sulphur was observed. The percentage compositions of the mixtures of sulphoxides were determined polarimetrically. The results are recorded in Table 1.

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