Studies on Conformation and Reactivity. Part XI.[1] Photochemical Oxidation, Ozonolysis, and Rearrangement of 5′,6′-Dihydrocholesta-3,5-dieno[3,4-*b*][1,4]oxathiin

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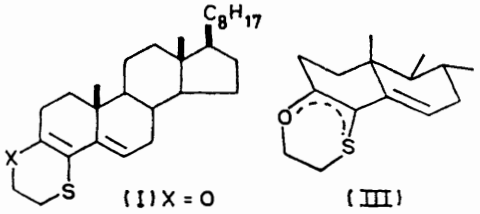
The 3,4-double bond of the delocalized *p*-electron system in 5′,6′-dihydrocholesta-3,5-dieno[3,4-*b*][1,4]oxathiin (I) shows a specific reactivity towards photo-oxidation and ozonolysis. Photo-oxidation of the oxathiin (I) gives 3,4-secocholest-5-eno[3,4-*b*][1,4]oxathian-3,4-dione (IV) under anhydrous conditions, but when water is present, in addition to (IV), 6β-hydroxy-4-(2-hydroxyethylthio)cholest-4-en-3-one (V) is produced. Ozonolysis of the oxathiin (I) affords similar results, giving the seco-dione (IV), 6β-ethoxy- (XVII) and 6β-acetoxy- (XXII) 4-(2-hydroxyethylthio)cholest-4-en-3-one, and 6β-ethoxy- (XIX) and 6β-acetoxy- (XXI) 3α-hydroxycholest-4-eno[3,4-*b*][1,4]oxathian 4′-oxide [derived from (XVII) and (XXII), respectively], depending on the conditions. The dehydrated analogue of the enone (V), 4-(2-hydroxyethylthio)cholesta-4,6-dien-3-one (XVI), is also isolated after ozonolysis.

PREVIOUS work in this laboratory produced a convenient synthesis of 5′,6′-dihydrocholesta-3,5-dieno[3,4-*b*][1,4]oxathiin [2] (I) and its 1,4-dithiin analogue (II) by the polyphosphoric acid (PPA)-catalysed ring opening of 4β,5-epoxy-5β-cholestan-3-one with 2-mercaptoethanol or ethanedithiol as the nucleophilic reagent.[3] In their



(I) X = O
(II) X = S
(III)

u.v. spectra, these compounds exhibited two characteristic bands, at 223 and 270 nm for the oxathiin (I) and at 240 and 292 nm for the dithiin (II). It has been indicated [2] that the chromophores giving rise to the bands at 270 and 292 nm are the 4-thio-substituted and 3,4-dithio-substituted 3,5-diene systems, respectively. Our earlier investigation [4] into the origin of other bands (223 and 240 nm) proved that these absorptions were due to conjugation of the delocalized *p*-electron system present in the ·O·C(3):C(4)·S· or ·S·C(3):C(4)·S· chromophores in the fixed half-chair conformation of the oxathian or dithian rings (III).

It then appeared to us that the 3,4-double bond in the 3,5-diene system of (I) and (II) might show characteristic photochemical behaviour. The present paper deals with the photo-oxidation and ozonolysis of the oxathiin (I), which proceeded *via* selective addition of the reagents to the 3,4-double bond (possibly from the α-side) followed by rearrangement of the 5,6-double bond and a preferential β- (axial) attack at C-6 (stereoelectronic requirements) of a suitable nucleophile.[5]

Photo-oxidation.—A solution of the oxathiin (I) in 1% aqueous ether was exposed to sunlight in the presence of air; the reaction was complete after 23 h (by t.l.c.) Chromatography of the crude product over silica gel gave 3,4-secocholest-5-eno[3,4-*b*][1,4]oxathian-3,4-dione (IV) and 4-(2-hydroxyethylthio)-6β-hydroxycholest-4-en-3-one (V) in 9·0 and 40·4% yield, respectively (see Scheme 1). When anhydrous solvents were used for the reaction, the seco-dione (IV) was the only isolable product; the formation of the ketone (V) could be detected only by t.l.c. Irradiation of the oxathiin (I) with a high-pressure mercury lamp gave similar results. When the irradiations were carried out under nitrogen, however, no reaction took place. Results of the irradiations are summarized in Table 1.

The structure of the seco-dione (IV) was verified by mass, i.r., u.v., and n.m.r. spectroscopic and microanalytical data. The presence of both a lactone and an unsaturated thiolactone group was evident from the u.v. and i.r. spectra. Each of four protons of the ·O·CH_2·CH_2·S· group showed a characteristic multiplet in the n.m.r. spectrum. The fact that oxygen added specifically to the 3,4-double bond was further supported by an n.m.r. signal assigned to the vinylic 6-proton. The fragmentation pattern in the mass spectrum of the 3,4-seco[3,4-*b*][1,4]oxathian-3,4-dione system (shown in Scheme 2) was further support for the structure.

Desulphurization of the seco-dione (IV) with Raney nickel afforded ethyl 4-oxo-3,4-secocholest-5-en-3-oate (VI) (see Scheme 1), which was identified as its 2,4-dinitrophenylhydrazone (VII) (45·0%), and by its conversion into the 3-ethyl ester of the 3,4-dioic acid (VIII) by aerial oxidation (21·9%). The assignment of the structures of the compounds (VII) and (VIII) was supported by microanalytical and spectroscopic data. Both seco-dione (IV) and diacid (VIII) gave, on alkaline hydrolysis, the free dioic acid (IX) (in 59·3 and 58·5% yield, respectively), which was characterized by comparison with an authentic specimen.[6]

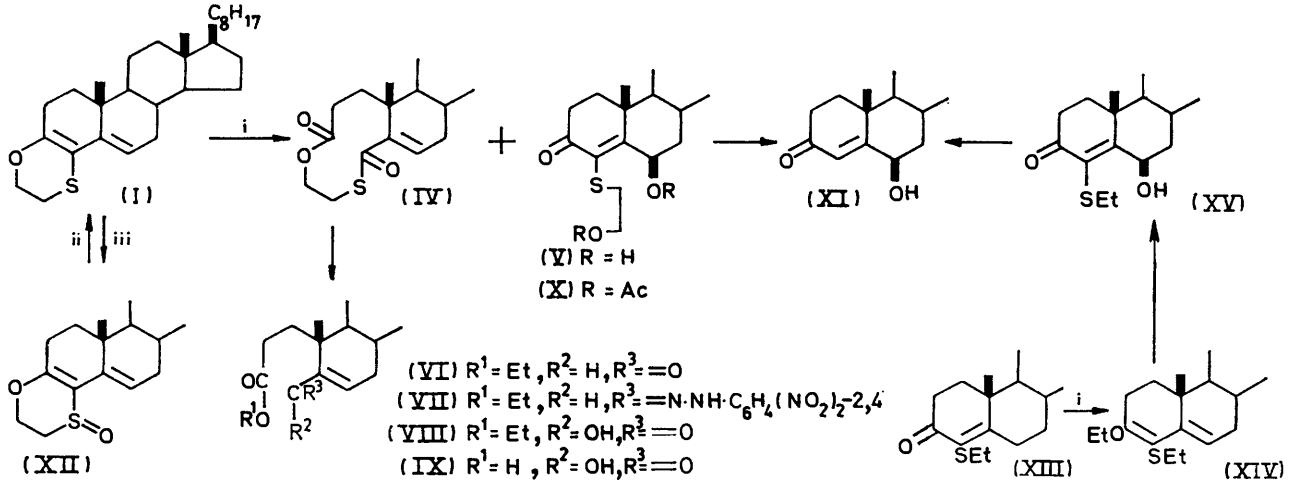
[1] Part X, T. Koga and S. Kawashima, *Chem. and Pharm. Bull.* (*Japan*), 1971, **20**, 21.
[2] L. F. Fieser, C. Yuan, and T. Goto, *J. Amer. Chem. Soc.*, 1961, **82**, 1996.
[3] M. Tomoeda, M. Ishizaki, H. Kobayashi, S. Kanatomo, T. Koga, M. Inuzuka, and T. Furuta, *Tetrahedron*, 1965, **21**, 733.
[4] A. Ishida, Y. Hiyoshi, T. Koga, and M. Tomoeda, *Chem. and Pharm. Bull.* (*Japan*), 1969, **17**, 255.
[5] Preliminary communication, A. Miyake and M. Tomoeda, *Chem. Comm.*, 1970, 240.
[6] O. Diels and E. Abderhalden, *Ber.*, 1903, **36**, 3177; L. F. Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4386.

The assignment of the structure and configuration at C(6) of the enone (V) (the m.p. covered an unusually wide range for a steroid, 168—183°) as a steroid was fully supported by microanalytical and spectroscopic data. The presence of the 4-thio-substituted 4-en-3-one system was indicated by the u.v. and i.r. spectra. Further, the i.r. spectrum supported the presence of hydroxy-groups. One of these groups was shown by the n.m.r. spectrum to be at C(6) with the β-configuration: the 10-methyl resonance was shifted downfield due to the deshielding effect of the cisoid hydroxy-group; further, the 6α-H resonance was deshielded [7] by the alkylthio-group and shifted to lower field. The n.m.r. spectrum also exhibited two characteristic multiplets assignable to the $HO{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}$ group at C(4). The mass spectral fragmentation patterns, in particular the peaks due to loss of 2 molecules of water, were further support for the structure.

Acetylation of the 4-thio-4-en-3-one (V) gave the diacetate (X), and desulphurization with Raney nickel gave 6β-hydroxycholest-4-en-3-one (XI) in 80·7% yield (characterized by comparison with an authentic specimen [8]).

It has been reported that oxidation of 3,4,5,6,7,8-hexahydro[1]benzopyran with *m*-chloroperbenzoic acid gave the corresponding ring-opened oxacyclodecanedione.[9] This result suggested that the oxathiin (I) might be also oxidized by such a reagent to give the seco-dione (IV). However, treatment of the oxathiin (I) with either the above peroxyacid or 30% hydrogen peroxide gave only the corresponding sulphoxide (XII), in high yield. The presence of the sulphoxide group in the product was supported by the i.r. spectrum and mass spectral fragmentation patterns, including an $M^+ - O$ peak. The results of microanalysis and the rest of the physical properties were consistent with the structure. Treatment of the sulphoxide (XII) with Raney nickel gave the original oxathiin (I) in 75·5% yield. Further, it was shown by a preliminary experiment that treatment of the sulphoxide (XII) with an excess of *m*-chloroperbenzoic acid does not cause oxidative cleavage of the C(3):C(4) bond to give a product of 3,4-seco-3,4-dione-type but gives the corresponding sulphone (unpublished data). This therefore excluded the possibility of forming the seco-dione (IV) by oxidation with hydrogen peroxide or such reagents generated secondarily during the reaction.

Gardi and Lusignani [10] have reported that the photo-oxidation of 3-ethoxycholesta-3,5-diene and its



Reagents: i, *hν*; ii, Raney Ni; iii, *m*-chloroperbenzoic acid.

SCHEME 1

TABLE 1

Yields (%) of photo-oxidation products from the oxathiin (I) [a]

Expt.	Light source	Solvent	Time	*T*/°C	Products (IV)	Products (V)
1	Sun	Wet ether [b]	29·5 h	r.t.	9·0	40·0
2	Sun	4 : 1 Acetone–ether	61 h	r.t.	36·9	Trace
3	Sun	Wet ether [b]	29·5 h	r.t.	No reaction	
4	Sun	4 : 1 Acetone–ether	23 h	r.t.	No reaction	
5	U.v. lamp	Wet ether [b]	80 min	−5 to −10	17·3	8·7
6	U.v. lamp	4 : 1 Acetone–ether	15 min	−5 to −10	33·8	

[a] Irradiations were carried out under air except for expts. 3 and 4, which were carried out under nitrogen. Yields are calculated assuming that 1 mol of products is formed from 1 mol of oxathiin (I); r.t. denotes room temperature. [b] 1% Aqueous ether.

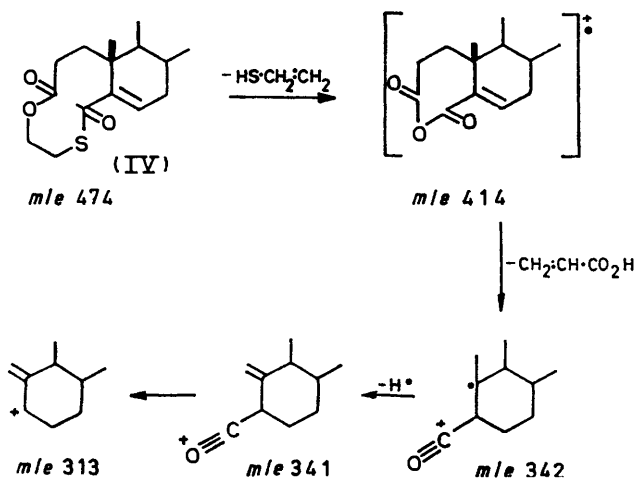
[7] M. Tomoeda, M. Inuzuka, T. Furuta, M. Shinozuka, and T. Takahashi, *Tetrahedron*, 1968, **24**, 959.

[8] L. F. Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4377.

[9] I. J. Borowitz and G. Gonis, *Tetrahedron Letters*, 1964, 1151.

[10] R. Gardi and A. Lusignani, *J. Org. Chem.*, 1967, **32**, 2647.

analogues gave the hydroxy-enone (XI) as the major product. Accordingly, 3-ethoxy-4-ethylthiocholesta-3,5-diene (XIV), prepared from 4-ethylthiocholest-4-en-3-one [3] (XIII), was photo-oxidized in aqueous ether with sunlight. 4-Ethylthio-6β-hydroxycholest-4-en-3-one (XV) was obtained as an only isolable product

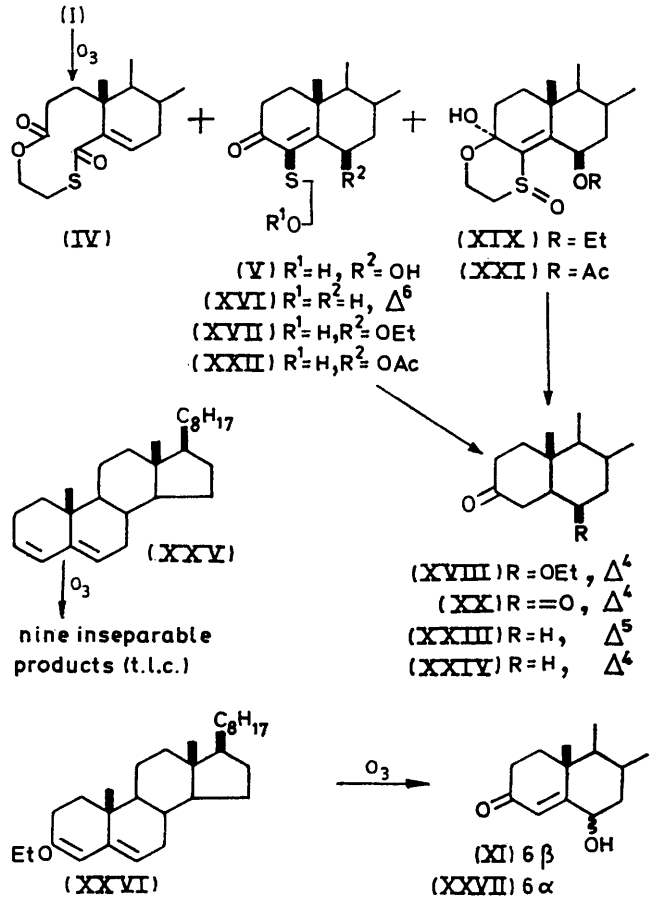


SCHEME 2

(19·3% yield). The presence of the 6β-hydroxy-function was established by n.m.r., as for the enone (V). The microanalytical and the other spectroscopic data were in full agreement with the structure. The fact that the thio-enone (XV), on desulphurization with Raney nickel gave the enone (XI) in 70·7% yield further supported the structure assigned to the thio-enone (XV). On the other hand, (XV) was not formed when (XIII) was similarly irradiated.

Ozonolysis.—The successful photo-oxidation of the oxathiin (I) prompted us to investigate the ozonolysis of this compound in order to see if ozone would add stereospecifically to the 3,4-double bond, as does oxygen. Investigations on the ozonolysis of unsaturated steroids

(a) *Products obtained with chloroform as solvent.* Two of the three products isolated were characterized



SCHEME 3

as the seco-dione (IV) and the thio-enone (V), which were also obtained from the photo-oxidation. The pale yellow, third product was identified by microanalytical and spectroscopic data as 4-(2-hydroxyethylthio)-cholesta-4,6-dien-3-one (XVI). The u.v. and n.m.r. spectra supported the presence of the conjugated 4,6-dienone system with a thio-function at the 4-position. The presence of the HO·CH_2·CH_2·S· group at C(4) was also indicated by the n.m.r. spectrum (characteristic multiplets) and the mass spectrum (in

TABLE 2

Yields (%) of ozonization products from the oxathiin (I) [a]

Expt.	Solvent	t/min	Products (IV)	(V)	(XVI)	(XVII)	(XIX)	(XXI)	(XXII)
1	Chloroform	30	22·6	8·7	22·1				
2	Chloroform–absolute ethanol [b]	25	12·0			26·9	19·7		
3	Chloroform–ethyl acetate–acetic acid [c]	17	14·6	7·3				9·3	23·0

[a] Ozonizations were carried out between −68 and −70°. [b] 4 : 1. [c] 50 : 50 : 1.

have hitherto been confined to monoene [11] and conjugated enone [12] systems. The ozonolysis of oxathiin (I) between −68 and −70° was carried out in chloroform, chloroform–absolute ethanol (4 : 1), or chloroform–ethyl acetate–acetic acid (50 : 50 : 1). The ozonides formed were decomposed with 6% hydrogen peroxide, giving predominantly neutral products (see Table 2). The products thus obtained were characterized as follows.

[11] C. Djerassi (ed.), 'Steroid Reactions,' Holden-Day, San Francisco, 1963, p. 428.

[12] E. Capsi, W. Schmid, and B. T. Khan, *Tetrahedron*, 1962, **18**, 767; E. Capsi, B. T. Khan, and S. N. Balasubrahmanyam, *ibid.*, p. 1013; O. R. Rodig and G. Zanati, *J. Org. Chem.*, 1968, **33**, 914.

particular the $M^+ - H_2O$ peak). The i.r. spectrum lent further support to the presence of the hydroxy-group.

(b) *Products obtained with chloroform–absolute ethanol as solvent.* One of the three products isolated was characterized as the seco-dione (IV). The second product obtained was identified (microanalysis and spectroscopy) as the 6β-ethoxy-analogue of (V), *i.e.* (XVII). The presence of a 6β-ethoxy-function was deduced from the n.m.r. spectrum using the same argument as applied to the hydroxy-function in (V). The fact that desulphurization of (XVII) with Raney nickel afforded 6β-ethoxycholest-4-en-3-one (XVIII) [13] in 61·4% yield was further support for the assigned structure.

The third product was shown to be 6β-ethoxy-3α-hydroxycholest-4-eno[3,4-*b*][1,4]oxathian 4-oxide (XIX) from microanalytical, mass spectral, and spectroscopic data as follows. The i.r. and u.v. spectra showed the presence of a hydroxy-group and a non-conjugated double bond. The i.r. spectrum also showed an absorption characteristic of the sulphoxide group. The n.m.r. spectrum exhibited characteristic peaks due to the 6β-ethoxy-group and the oxathiin ring; the multiplet signal of one of the 6′-protons was *ca.* 1 p.p.m. downfield from the peak due to the other proton of the same group. This suggested the presence of a 3-hydroxy-function with an α-configuration in a 1,3-diaxial-type relationship [14] with the lower-field proton. The n.m.r. spectrum also showed that the 10-methyl peak was deshielded by the 6β-ethoxy function, and that the 6α-H was deshielded by the sulphoxide function at the 4-position [*cf.* the analogous effect of the 4-thio-function in the enone (V)]. Desulphurization of the oxathian (XIX) afforded the expected 6β-ethoxy-4-en-3-one (XVIII) in 48·0% yield, while treatment with 10% ethanolic potassium hydroxide afforded cholest-4-ene-3,6-dione [8] (XX) (56·3% yield). This latter reaction can be explained by an allylic rearrangement, followed by the nucleophilic attack of an hydroxide ion at the 6-position, then finally the elimination of the sulphoxide group. The sulphoxide (XIX) was formed from the hydroxyethylthio-compound (XVII) in moderately high yields by treatment with 30% hydrogen peroxide in acetic acid or with *m*-chloroperbenzoic acid. The mechanism requires oxidation of the thio-function of (XVII) followed by intramolecular cyclization at C(3). These results establish the relationship between (XVII) and (XIX).

(c) *Products obtained with chloroform–ethyl acetate–acetic acid as solvent.* Two of the four products isolated were the seco-dione (IV) and the thio-enone (V). The third product was identified as the 6β-acetoxy-analogue (XXI) of the oxathian (XIX). The structure of the compound was fully supported by the spectroscopic evidence (i.r., n.m.r., and mass).

The fourth product was characterized as the 6β-acetoxy-analogue (XXII) of the enone (V) [*cf.* the case of the 6β-ethoxy-compound (XVII)]. The presence of the 6β-acetoxy-group was verified by mass, i.r., and n.m.r. spectra. Treatment of the acetate (XXII) with *m*-chloroperbenzoic acid gave the oxathian (XXI) in 57·2% yield, thus establishing the structural relationship of these two compounds as in the case of the ethoxy-compound (XVII) and the oxathian (XIX). The acetate (XXII) gave the acetate (X) on treatment with acetic anhydride–pyridine. However, desulphurization of the 6β-acetoxy-compounds (XXI) and (XXII) gave unusual results, different from those with the 6β-ethoxy-compounds (XVII) and (XIX). Desulphurization of the acetates (XXI) or (XXII) was accompanied by the elimination of the acetoxy-group, yielding cholest-5-en-3-one [15] (XXIII) in 40·7% yield from (XXI), or the 5-en-3-one (XXIII) and cholest-4-en-3-one [15] (XXIV) in 35·9 and 15·2% yields, respectively from (XXII).

To elucidate the mechanisms of the photo-oxidation and ozonolysis of the oxathiin (I), ozonolysis of cholesta-3,5-diene [16] (XXV) and its 3-ethoxy-analogue [17] (XXVI), that is the corresponding compounds without any 4-thio-function, was carried out. Although ozonolysis of the diene (XXV) failed to give any isolable crystalline product, treatment of the ethoxy-diene (XXVI) with ozone at −20° in 4 : 1 chloroform–absolute ethanol gave the enone (XI) and its 6α-hydroxy-isomer (XXVII) in 33·1 and 18·8% yield, respectively (see Scheme 3). The structure of the enone (XI) was established by its physical properties and by comparison with an authentic specimen.[8] The assignment of structure (XI) was based on microanalytical and spectral data. The i.r. and u.v. spectra were consistent with the 4-en-3-one system having a hydroxy-function at C(6). The n.m.r. spectrum showed the 10-methyl peak at higher field than δ 0·8,[18] and also a broad multiplet due to the axial 6β-proton, thus indicating that the hydroxy-function was at C(6), with an α-configuration.

DISCUSSION

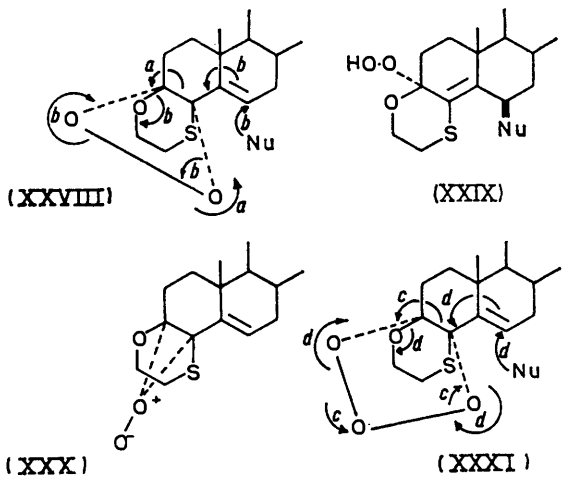
The fact that the production of the seco-dione (IV) from the oxathiin (I) required both oxygen and light indicates that the reaction is a photo-oxidation. The formation of the products may be explained by the selective addition of oxygen molecule in the singlet state [19,20] to the 3,4-double bond (probably from the less hindered α-side), forming a 1,2-dioxetan [20] (XXVIII) in the transition state. Cleavage of the peroxide and 3,4-bonds according to route (*a*) in Scheme 4 would then give the seco-dione (IV). On the other hand, a

[13] T. Koga and M. Tomoeda, unpublished data.
[14] K. Tori and T. Komeno, *Tetrahedron*, 1965, **21**, 322.
[15] W. Lwowski, T. J. Maricich, and T. W. Mattingly, jun., *J. Amer. Chem. Soc.*, 1965, **87**, 1947.
[16] H. E. Stavely and W. Bergmann, *J. Org. Chem.*, 1937, **1**, 567.
[17] D. L. Juliane, E. W. Meyer, W. J. Karpel, and W. Cole, *J. Amer. Chem. Soc.*, 1951, **73**, 1982.
[18] N. S. Bhacca and D. H. Williams, ' Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 13.
[19] C. S. Foote and S. Wexler, *J. Amer. Chem. Soc.*, 1964, **86**, 3879; C. S. Foote, S. Wexler, and W. Ando, *Tetrahedron Letters*, 1965, 411.
[20] W. Fenical, D. R. Kearns, and Ph. Radlick, *J. Amer. Chem. Soc.*, 1969, **91**, 3396, 7772.

series of bond migrations and cleavages concerted with an attack at C(6) by water (a suitable nucleophile present in the mixture) as shown by route (*b*), would give a hydroperoxide (XXIX). The hydroperoxide (XXIX) might be then reduced photochemically by solvent to give the thio-enone (V). Another possibility, that the products could be derived *via* a perepoxide (XXX),[20] cannot be excluded. The fact that the 6-hydroxy-compound (V) has the thermodynamically less stable axial β-configuration at the allylic 6-position can be understood by the inspection of stereomodels. These suggest that stereoelectronic requirements [21] around C(6) favour the maximum overlap of the *p* orbital of the oxygen atom of H_2O with the vacant *p* orbital at C(6) from the β- or axial side.

A photosensitized oxidation with singlet state oxygen as an electrophilic reagent has been reported.[22] The oxathiin (I) itself might behave as a photosensitizer for the generation of singlet oxygen in the photo-oxidation.

The mechanism of the ozonolysis of the oxathiin (I) is probably similar to that of the photo-oxidation. A likely transition state is the ozonide (XXXI), formed by the addition of ozone to the 3,4-double bond from the α-side. The explanation for the formation of the products from the ozonide (XXXI) follows analogously from that of the photolysis of the dioxetan (XXVIII). Bond cleavage, according to route (*c*), would give the



SCHEME 4

seco-dione (IV); a series of bond cleavages and migrations concerted with nucleophilic attack of solvent molecules, *i.e.* H_2O, EtOH, or AcOH, at C(6) from the β- (axial) side (stereoelectronic requirements) would give the 6-oxy-compounds (V), (XVII), and (XXII). Furthermore, the successful conversion of the 6-ethoxy-enone (XVII) to the oxathian oxide (XIX) under oxidative conditions leads to the conclusion that the oxathian oxide-type products with the 3α-hydroxy-group, *i.e.* (XIX) and (XXI), were derived secondarily from (XVII) and (XXII). These latter compounds were formed first during the reaction, by oxidation of the sulphide at C(4) to the sulphoxide (with the hydrogen peroxide generated from the decomposition of the intermediate ozonide), followed by spontaneous cyclization at C(3).

Recently, Kirk and Wiles reported that the oxidation of 3-alkoxy-steroid 3,5-dienes by peroxy-acid takes place mainly at the 3,4-bond under anhydrous conditions but at C(6) in the presence of water.[23] They suggested that the behaviour on peroxy-acid oxidation appears attributable to the dienol ether system, and is independent of any effect due to the sulphur atom at C(4). It is therefore surprising to note that the peroxy-acid oxidation of the oxathiin (I) gave the corresponding sulphoxide (XII) or further oxidized sulphone only. It may then be concluded that the delocalized *p* electron system (λ 223 nm) of the oxathiin (I) is specifically sensitive to both photo-oxidation and ozonolysis.

EXPERIMENTAL

M.p.s were taken on a Kofler-type hot-stage apparatus. Values of $[\alpha]_D$ refer to solutions in $CHCl_3$; u.v. absorption spectra were measured for solutions in 95% EtOH, and i.r. spectra for Nujol mulls, unless otherwise stated. N.m.r. spectra were measured for solutions in [^{2}H]chloroform on Varian Associates HA-100 or A-60 high resolution spectrometers or a JEOL C-60H high-resolution instrument. Mass spectroscopic analysis was performed with a JEOL JMS-01SG double-focusing spectrometer, and the spectra were analysed mainly in the millimass order. Silica gel (Kanto Chemical Co.) was used for chromatographic separations. Irradiation was carried out in Pyrex flasks either under sunlight or with a 300 W mercury lamp, under dry air or oxygen-free nitrogen. Aqueous ether, for the photo-oxidations, refers to water-saturated peroxide-free ether.

5′,6′-Dihydrocholesta-3,5-dieno[3,4-b][1,4]*oxathiin* (I).—This compound was synthesized according to the procedure of Tomoeda *et al.*;[3] m.p. 154—155·5°, $[\alpha]_D^{30}$ −162° (*c* 0·55), $\lambda_{max.}$ (n-hexane) 223 (ε 9300) and 270 nm (8800), $\nu_{max.}$ 1630w and 1613w cm^{-1} (conj. diene), τ 4·48 (1H, m, 6-H), 5·48—6·09 (2H, m, O·CH_2·CH_2·S·), 6·89—7·18 (2H, m, ·S·CH_2·CH_2·O·), 9·00 (3H, s, 19-H_3), and 9·30 (3H, s, 18-H_3).

Photo-oxidation of the Oxathiin (I).—(i) *With sunlight in aqueous ether under air.* A solution of oxathiin (I) (500 mg) in aqueous ether (50 ml) was exposed under air to sunlight at room temperature for 29·5 h. The solution was concentrated *in vacuo* to give pale yellow crystals (561 mg), m.p. 73—86°, which were chromatographed over silica gel (56 g). Elution with benzene (120 ml) gave 3,4-*seco-cholest-5-eno*[3,4-b][1,4]*oxathian-3,4-dione* (IV) as needles (49 mg, 9·0%), m.p. 133—134·5° (from MeOH) (Found: C, 73·2; H, 9·95; S, 6·8. $C_{29}H_{46}O_3S$ requires C, 73·35; H, 9·75; S, 6·75%), $[\alpha]_D^{26}$ +26·1° (*c* 0·76), $\lambda_{max.}$ 238 nm (ε 7100), $\nu_{max.}$ 3020w (C=CH), 1740s (O·CO), 1645s (S·CO·C=C), and 1620w cm^{-1} (C=C), τ 3·37 (1H, m, 6-H), 5·04—5·24 and 6·16—6·39 (1H each, m, O·CH_2), 6·51—6·76 and

[21] N. L. Allinger and E. L. Eliel, (eds.) 'Topics in Stereochemistry,' Wiley, New York, 1967, vol. 2, p. 163.

[22] K. P. Kopecky and H. J. Reich, *Canad. J. Chem.*, 1966, **43**, 2265; T. Wilson, *J. Amer. Chem. Soc.*, 1966, **88**, 2898.

[23] D. N. Kirk and J. M. Wiles, *Chem. Comm.*, 1970, 518.

6·94—7·18 (1H each, m, S·CH_2), 8·69 (3H, s, 19-H_3), and 9·30 (3H, s, 18-H_3), *m/e* 474·316 ($C_{29}H_{46}O_3S$) (M^+), 414·311 ($C_{27}H_{42}O_3$) (M^+ — HS·CH:CH_2), 342·294 ($C_{24}H_{38}O$) (414 — CH_2:CH·CO_2H), 341·286 ($C_{24}H_{37}O$) (342 — H), and 313·289 ($C_{23}H_{37}$) (341 — CO).

Further elution with 2 : 1 benzene–ether (300 ml) gave 6β-*hydroxy*-4-(2-*hydroxyethylthio*)*cholest*-4-*en*-3-*one* (V) as needles (218 mg, 40·0%), m.p. 168—183° (from MeOH) (Found: C, 72·85; H, 10·35; S, 6·6. $C_{29}H_{48}O_3S$ requires C, 73·05; H, 10·15; S, 6·75%), $[\alpha]_D^{26}$ +30·9° (*c* 0·87), $\lambda_{max.}$ 247 (ε 9300) and 320 nm (1600), $\nu_{max.}$ 3400s (OH), 1675s (CO·C:C), and 1550 cm^{-1} (C=C), τ 4·20 (1H, m, 6-H), 6·10—6·35 (3H, m, OH and O·CH_2), 7·18—7·60 (3H, m, OH and S·CH_2), 8·60 (3H, s, 19-H_3), and 9·26 (3H, s, 18-H_3), *m/e* 476·330 ($C_{29}H_{48}O_3S$) (M^+).

In a control experiment, oxathiin (I) (500 mg) was kept in wet ether (50 ml) in the dark at room temperature under air for 33 days. The mixture, on removal of the solvent *in vacuo* followed by work-up of the crude product (m.p. 127—154°, 513 mg), gave the starting material (I), m.p. 153—154° (320 mg, 64·0%), and the enone (V) (92 mg, 17·0%), m.p. 163—183°.

(ii) *With sunlight in acetone–ether* (4 : 1) *under dry air.* Photo-oxidation of the oxathiin (I) (500 mg) in acetone–ether (50 ml, 4 : 1 v/v) under sunlight and dry air for 61 h gave the seco-dione (IV) (198 mg, 36·9%), m.p. and mixed m.p. 133—135° (from methanol). No detectable amounts of the enone (V) were obtained.

(iii) *With a high-pressure mercury lamp in wet ether under air.* Photo-oxidation of the oxathiin (I) (500 mg) in wet ether (100 ml) with a 300 W high-pressure mercury lamp under air between −5 and −10° for 80 min gave the seco-dione (IV) (93 mg, 17·3%), m.p. and mixed m.p. 134—135·5° (from methanol) and the enone (V) (48 mg, 8·7%), m.p. and mixed m.p. 163—182·5° (from methanol).

(iv) *With a* 300 W *mercury lamp in acetone–ether* (4 : 1) *under dry air.* Irradiation of a solution of the oxathiin (I) (500 mg) in 4 : 1 acetone–ether (150 ml) with a 300 W mercury lamp between −5 and −10° under dry air for 15 min gave the seco-dione (IV) (33·8%), m.p. 132—134°, in addition to the starting material (I) (16 mg, 3·2%).

(v) *With sunlight in either acetone–ether* (4 : 1) *or in wet ether under nitrogen.* Photo-oxidation of the oxathiin (I) (500 mg) in acetone–ether (50 ml; 4 : 1) under sunlight and nitrogen for 23 h gave the starting material (I) (453 mg, 90·6%), m.p. and mixed m.p. 153—154° (from ether–acetone), as the sole product. Similar results were obtained with wet ether: only oxathiin (I) was recovered in high yield (74·8%).

Desulphurization of the Seco-dione (IV) *with Raney Nickel.*—To a solution of the seco-dione (IV) (200 mg) in ethyl acetate (40 ml), Raney nickel (*ca.* 3 g) (prepared as reported [24] and deactivated by heating for 15 min first in ethyl acetate then in acetone under reflux) was added and the suspension was heated under reflux for 3 min. The mixture was filtered, and the filtrate evaporated to give *ethyl*-4-*oxo*-3,4-*secocholest*-5-*en*-3-*oate* (VI), an oil (122 mg), which gave [25] the 2,4-*dinitrophenylhydrazone* (VII), orange crystals (126 mg, 45·0%), m.p. 161·5—163° (from methanol–ether) (Found: C, 67·25; H, 8·4; N, 8·75. $C_{35}H_{52}N_4O_6$ requires C, 67·3; H, 8·4; N, 8·95%), $[\alpha]_D^{24}$ −119·4° (*c* 1·07); $\lambda_{max.}$ 380 nm (ε 28,000), $\nu_{max.}$ 3270m, 3100w, 1511s (NH), 1730s (CO_2Et), and 1620s cm^{-1} (CH=N), τ −1·01 (1H, s, CH=N), 0·99 (1H, d, *J* 3 Hz, 3′-H of benzene nucleus), 1·67 (1H, q, *J* 3 and 6 Hz, 5′-H of benzene nucleus), 2·15 (1H, d, *J* 6 Hz, 6′-H of benzene nucleus), 2·37 (1H, s, NH=N), 3·67 (1H, m, 6-H), 5·93 (2H, q, *J* 7·2 Hz, O·CH_2-Me), 7·92 (2H, s, 7-H_2), 8·72 (3H, s, 19-H_3), 8·85 (3H, t, *J* 7·2 Hz, O·CH_2*Me*), and 9·28 (3H, s, 18-H_3).

3-*Ethyl* 4-*Hydrogen* 3,4-*Secocholest*-5-*en*-3,4-*dioate* (VIII).—Treatment of the seco-dione (IV) (400 mg) with Raney nickel (*ca.* 6 g) in ethyl acetate (80 ml) was carried out as before to give the ester (VI) as an oil (252 mg), which was dissolved in benzene (40 ml), and heated under reflux for 16 h in a stream of dry air. The solution was concentrated *in vacuo* to give an oily residue (274 mg). Chromatography (silica gel, 27 g) with benzene–ether (140 ml) as eluant gave the *half ester* (VIII), prisms (85 mg, 21·9%), m.p. 142—144·5° (from methanol) (Found: C, 75·85; H, 10·75. $C_{29}H_{48}O_4$ requires C, 75·6; H, 10·5%), $[\alpha]_D^{22}$ −42·0° (*c* 0·28), $\lambda_{max.}$ 215 nm (ε 12,500), $\nu_{max.}$ 3000s (OH), 1735s (CO_2H), 1685s (C:C·CO_2H), and 1628m (C=C), τ 2·84 (1H, m, 6-H), 5·89 (2H, q, *J* 7·2 Hz, O·CH_2Me), 8·77 (3H, t, *J* 7·2 Hz, O·CH_2*Me*), 8·79 (3H, s, 19-H_3), and 9·30 (3H, s, 18-H_3).

Alkaline Hydrolysis of the Half Ester (VIII).—A solution of the half ester (VIII) (46 mg) and sodium hydroxide (10 mg) in aqueous 90% methanol (3 ml) was heated under reflux for 7 h. The solution was added to water (10 ml) and acidified with aqueous 20% acetic acid, and the product was extracted into ether. The extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to leave 3,4-secocholest-5-ene-3,4-dioic acid (IX) as leaflets (25 mg, 58·5%), m.p. 283—286° (from aqueous methanol) identical with an authentic sample,[6] $\lambda_{max.}$ 215 nm (ε 9200), $\nu_{max.}$ 3000m (OH), 1702s, and 1693s cm^{-1} (CO_2H).

Alkaline Hydrolysis of the Seco-dione (IV).—A solution of the seco-dione (IV) (50 mg) and sodium hydrogen carbonate (100 mg) in aqueous 90% methanol (55 ml) was heated under reflux for 16·5 h. Work-up as described for the half-ester (VIII) gave the free acid (IX) as leaflets (27 mg, 59·3%), m.p. and mixed m.p. 283—286° (from aqueous methanol). I.r. and u.v. spectra were identical with those of an authentic sample.

Acetylation of the Enone (V).—The dihydroxy-compound (V) (148 mg) was dissolved in a mixture of acetic anhydride (1·5 ml) and pyridine (2 ml); the mixture was kept at room temperature for 42 h, then added to ice–water (50 ml). The product was extracted into ether. The extract was successively washed with aqueous saturated sodium hydrogen carbonate, water, aqueous 10% hydrochloric acid, and water, then dried (Na_2SO_4). Evaporation *in vacuo* left a yellow oily residue (213 mg). Chromatography over silica gel (10 g) with benzene–ether (40 ml, 9 : 1) gave 6β-*acetoxy*-4-(2-*acetoxyethylthio*)*cholest*-4-*en*-3-*one* (X) (119 mg, 68·4%) as a homogeneous oil (t.l.c.). The di-acetate crystallized gradually from methanol as needles (88 mg, 50·5%), m.p. 63—64·5° (from methanol) (Found: C, 71·05; H, 9·3; S, 5·7. $C_{33}H_{52}O_5S$ requires C, 70·7; H, 9·35; S, 5·7%), $[\alpha]_D^{26}$ +42·8° (*c* 0·50), $\lambda_{max.}$ 244 (ε 9000) and 319 nm (1900), $\nu_{max.}$ 1735s (CO_2Me), 1687s (CO·C:C), and 1565m cm^{-1} (C=C), τ 3·26 (1H, m, 6-H), 5·94 (2H, t, *J* 11 Hz, ·O·CH_2·CH_2·S·), 7·07 (2H, t, *J* 11 Hz, ·S·CH_2·CH_2·O·), 7·96 (6H, s, CO_2Me), 8·77 (3H, s, 19-H_3), and 9·25 (3H, s, 18-H_3).

Desulphurization of the Enone (V) *with Raney Nickel.*—To a solution of the enone (V) (136 mg) in acetone (30 ml), deactivated Raney nickel (*ca.* 2·7 g) was added and the

[24] R. Mozingo, *Org. Synth.*, 1955, Coll. Vol. III, 181.
[25] G. D. Johnson, *J. Amer. Chem. Soc.*, 1951, **73**, 5888.

suspension was heated under reflux for 5 min. The mixture was filtered, and the filtrate on removal of the solvent *in vacuo* gave crystals (117 mg), m.p. 164—172°, which were chromatographed over silica gel (12 g). Elution with benzene–ether (80 ml, 6 : 1) gave 6β-hydroxycholest-4-en-3-one (XI) as needles (92 mg, 80·7%), m.p. and mixed m.p.[8] 192—195° (from methanol). The u.v. and i.r. spectra were identical with those of an authentic specimen,[8] $[\alpha]_D^{22}$ +31·8° (*c* 0·22), $\lambda_{max.}$ 239 nm (ε 13,100), $\nu_{max.}$ 3360s (OH), 1670s, and 1612w cm^{-1} (CO·C:C).

Oxidation of the Oxathiin (I) *with Hydrogen Peroxide or* m-*Chloroperbenzoic Acid.*—Compound (V) (100 mg) was dissolved in ether (10 ml) saturated with aqueous 30% hydrogen peroxide, and the mixture was kept in the dark at room temperature for 24 h. After addition of 5 drops of aqueous 30% hydrogen peroxide, the mixture was kept in the dark at room temperature for a further 35 h, then added to ice–water; the product was extracted into ether. The extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to leave crystals (114 mg), m.p. 200—208°. Chromatography over silica gel (11·5 g) with benzene–ether (65 ml, 2 : 1) gave 5′,6′-*dihydrocholesta*-3,5-*dieno*[3,4-b][1,4]*oxathiin* 4′-*oxide* (XII) as fine crystals (69 mg, 66·6%), m.p. (decomp.) (from ether) 232—233·5° (Found: C, 76·2; H, 8·9; S, 6·9. $C_{29}H_{46}O_2S$ requires C, 75·95; H, 10·1; S, 7·0%), $[\alpha]_D^{19}$ −68·0° (*c* 0·96), $\lambda_{max.}$ 217 (ε 7000) and 241 nm (8800), $\nu_{max.}$ (KBr) 1640m, 1590s (C=C), 1040s cm^{-1} (SO), τ 3·82 (1H, m, 6-H), 5·54 (2H, m, O·CH_2), 7·10 (2H, m, S·CH_2), 9·10 (6H, s, 19- and 21-H_3), and 9·31 (3H, s, 18-H_3), *m/e* 458·324 ($C_{29}H_{46}O_2S$) (M^+) and 442·327 ($C_{29}H_{46}OS$) (M^+ − O).

Oxidation of the oxathiin (I) with *m*-chloroperbenzoic acid also gave the oxide (XII). To a solution of oxathiin (I) (100 mg) in dichloromethane (10 ml), *m*-chloroperbenzoic acid (44 mg, 1·1 mol. equiv.) was added, and the mixture was kept at room temperature for 3 h, washed with aqueous 10% sodium sulphite (5 ml), water, saturated aqueous sodium hydrogen carbonate, and water, and then dried (Na_2SO_4). Evaporation left the oxide (XII) (103 mg, 99·2%), m.p. and mixed m.p. 233—234° (decomp.) (from ether).

Reduction of the Oxide (XII) *with Raney Nickel.*—To a solution of the oxide (XII) (190 mg) in ethyl acetate (40 ml), deactivated Raney nickel (*ca.* 5·9 g) was added and the suspension was heated under reflux for 45 min. The mixture was filtered, and the filtrate, on removal of solvent *in vacuo*, gave needles (168 mg), m.p. 143—152°, which were chromatographed over silica gel (17 g). Elution with light petroleum–benzene (30 ml, 1 : 2) gave the oxathiin (I) (147 mg, 75·5%), m.p. and mixed m.p. 153—155° (from acetone–ether).

3-*Ethoxy*-4-*ethylthiocholesta*-3,5-*diene* (XIV).—To a solution of 4-ethylthiocholest-4-en-3-one (XIII) (1·0 g) in dioxan (5 ml), ethyl orthoformate (1 ml), 95% ethanol (0·05 ml), and conc. H_2SO_4–dioxan (0·25 ml) [prepared by addition of conc. H_2SO_4 (0·25 ml) to dioxan (10 ml)] were added, and the mixture was kept at room temperature for 16 h. After addition of pyridine (1 ml), the mixture was concentrated *in vacuo* to give the diene (XIV) as pale yellow leaflets (946 mg, 89·0%), m.p. 146·5—147° (from acetone) (Found: C, 78·95; H, 11·25; S, 6·75. $C_{31}H_{52}OS$ requires C, 78·75; H, 11·1; S, 6·8%), $[\alpha]_D^{19}$ −110·3° (*c* 1·02), $\lambda_{max.}$ 242 nm (ε 23,400), $\nu_{max.}$ 1635m, 1573s [·O·C:C(·S·)·C:C] and 1035s cm^{-1} (C–S), τ 3·90 (1H, m, 6-H), 5·93—6·51 (2H, m, ·O·CH_2Me), 7·34—7·76 (2H, m, ·S·CH_2Me), 8·60—8·90 (6H, m, ·S·CH_2*Me* and ·O·CH_2*Me*), 9·12 (3H, s, 19-H_3), and 9·37 (3H, s, 18-H_3).

Photo-oxidation of the Diene (XIV) *with Sunlight.*—A solution of (XIV) (1·0 g) in wet ether (100 ml) was exposed to sunlight under air at room temperature for 40 h, and worked-up as described for the oxathiin (I), to give 4-*ethylthio*-6β-*hydroxycholest*-4-*en*-3-*one* (XV) as needles (188 mg, 19·3%), m.p. 154·5—155·5° (from methanol) (Found: C, 75·2; H, 10·4; S, 6·85. $C_{29}H_{48}O_2S$ requires C, 75·55; H, 10·5; S, 6·95%), $[\alpha]_D^{16}$ −1·3° (*c* 0·75), $\lambda_{max.}$ 247 (ε 9400) and 321 nm (3400), $\nu_{max.}$ 3470s (OH), 1668s [CO·C(·S·):C·], and 1540m cm^{-1} (C=C), τ 4·30 (1H, m, 6-H), 7·25—7·55 (2H, m, ·S·CH_2Me), 8·65 (3H, s, 19-H_3), 8·86 (3H, m, S·CH_2*Me*), and 9·32 (3H, s, 18-H_3); *m/e* 460·338 ($C_{29}H_{48}O_2S$) (M^+).

Desulphurization of the Enone (XV) *with Raney Nickel.*—Treatment of the enone (XV) (30 mg) with deactivated Raney nickel (*ca.* 0·6 g) in acetone (10 ml) and work-up of the mixture as described for the enone (V) gave the hydroxyenone (XI) (20 mg, 70·7 %), m.p. and mixed m.p. 193·5—195° (from methanol).

Ozonolysis of the Oxathiin (I).—(i) *In chloroform.* Ozonized oxygen was passed through a solution of the oxathiin (I) (1·0 g) in chloroform (30 ml) at between −68 and −70° for 30 min, then aqueous 6% hydrogen peroxide (12·5 ml) was added. The mixture was kept at room temperature for 20 h, and the product then extracted into ether. The extract was washed with aqueous N-sodium hydroxide (30 ml) and water, and then dried (Na_2SO_4). The solvent was removed *in vacuo* to give a yellow oily residue (1·062 g), which was chromatographed over silica gel (107 g). Elution with benzene (250 ml) gave the seco-dione (IV) (234 mg, 22·6%), m.p. and mixed m.p. 133·5—134° (from methanol).

Elution with benzene–ether (200 ml, 4 : 1) gave 4-(2-*hydroxyethylthio*)*cholesta*-4,6-*dien*-3-*one* (XVI) as pale yellow needles (234 mg, 22·1%), m.p. 73—76° (from ether–methanol) (Found: C, 75·25; H, 10·4; S, 7·35. $C_{29}H_{46}O_2S$ requires C, 75·95; H, 10·2; S, 7·0%), $[\alpha]_D^{22}$ +68·4° (*c* 0·94), $\lambda_{max.}$ 289 (ε 17,900) and 344 nm (4800), $\nu_{max.}$ 3340s (OH), 1654s [CO·C(·S·):C·], 1602m, and 1509w cm^{-1} (C=C), τ 2·71 (1H, q, *J* 10 and $J_{6,8}$ 3 Hz, 6-H), 3·68 (1H, q, *J* 10 and $J_{7,8}$ 2 Hz, 7-H), 6·47 (2H, t, *J* 5 Hz, O·CH_2·CH_2·S·), 7·22 (2H, t, *J* 5 Hz, ·S·CH_2·CH_2·O·), 8·87 (3H, s, 19-H_3), and 9·25 (3H, s, 18-H_3), *m/e* 458·321 ($C_{29}H_{46}O_2S$) (M^+).

Further elution with benzene–ether (100 ml, 3 : 1) gave the enone (V), m.p. 148—176° (one spot on t.l.c.; 91 mg, 8·7%). The needles were chromatographed over silica gel (18 g) and on elution with benzene–ether (54 ml, 2 : 1) gave compound (V) (87 mg, 8·3%), m.p. and mixed m.p. 165—183° (from light petroleum–ether).

The aqueous alkaline extract of the ethereal solution of the crude product was acidified with aqueous N-sulphuric acid, and the acidic products were extracted into ether. The extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to leave an oil (76 mg). The oil was not further examined.

(ii) *In chloroform–alcohol* (4 : 1). Ozonolysis of the oxathiin (I) (1·0 g) in this solvent (30 ml) was carried out as described in (i); an oily residue (1120 mg) was obtained from the neutral fraction of the product. The oil was chromatographed over silica gel (110 g) with benzene (300 ml) as eluant to give the seco-dione (IV) (132 mg, 12·0%), m.p. and mixed m.p. 132—134° (from methanol).

Elution with benzene–ether (300 ml, 4 : 1) gave 6β-*ethoxy*-4-(2-*hydroxyethylthio*)*cholest*-4-*en*-3-*one* (XVII) as

needles (305 mg, 26·9%), m.p. 102—103° (from aqueous methanol) (Found: C, 73·95; H, 10·45; S, 6·2. $C_{31}H_{52}O_3S$ requires C, 73·75; H, 10·4; S, 6·35%), $[\alpha]_D^{22}$ +21·0° (*c* 1·04), $\lambda_{max.}$ 246 (ε 8700) and 320 nm (1600), $\nu_{max.}$ 3350s (OH), 1677s [CO·C(·S·):C], and 1533w cm^{-1} (C=C), τ 4·60 (1H, m, 6-H), 6·43 (2H, t, *J* 5 Hz, ·S·CH_2·CH_2·OH), 6·67 (2H, q, *J* 6·5 Hz, ·O·CH_2Me), 7·23 (2H, t, *J* 5 Hz, ·S·CH_2·CH_2·OH), 8·69 (3H, s, 19-H_3), 8·86 (3H, t, *J* 6·5 Hz, ·O·CH_2*Me*), and 9·28 (3H, s, 18-H_3), *m/e* 504·361 ($C_{31}H_{52}O_3S$) (M^+).

Further elution with benzene–ether (900 ml, 4 : 1) gave 6β-*ethoxy*-3α-*hydroxycholest*-4-*eno*[3,4-b][1,4]*oxathian* 4′-*oxide* (XIX) as prisms (237 mg, 19·7%), m.p. 123—124° (from aqueous acetone) (Found: C, 71·5; H, 10·15; S, 6·35. $C_{31}H_{52}O_4S$ requires C, 71·5; H, 10·05; S, 6·15%), $[\alpha]_D^{22}$ −9·6° (*c* 1·05), $\lambda_{max.}$ 205 nm (ε,10,700), $\nu_{max.}$ 3320s (OH), 1603m (C=C), 1080s (·O·), and 1065s cm^{-1} [·S(O)·], τ 4·89—5·16 (1H, m, ·S·CH_2·CH_AH_B·O·), 5·21 (1H, m, 6-H), 6·12 (1H, m, ·S·CH_2·CH_AH_B·O·), 6·67—7·11 (4H, m, ·S·CH_2·CH_2·O· and ·O·CH_2Me), 8·83 (3H, s, 19-H_3), 8·87 (3H, t, *J* 6·5 Hz, ·O·CH_2*Me*), and 9·13 (3H, s, 18-H_3), *m/e* 520·361 ($C_{31}H_{52}O_4S$) (M^+).

The acidic products, obtained as an oil (101 mg), were not further investigated.

(iii) *In chloroform–ethyl acetate–acetic acid* (50 : 50 : 1). Ozonolysis of the oxathiin (I) (1·0 g) in this solvent system (30·35 ml) was carried out as described in (i); an oily residue (1·107 g) was obtained from the neutral fraction of the product. This was chromatographed over silica gel (220 g) with benzene (300 ml) as eluant to give the seco-dione (IV) (157 mg, 14·6%), m.p. and mixed m.p. 133·5—135° (from methanol).

Elution with benzene–ether (180 ml, 4 : 1) gave 6β-*acetoxy*-3α-*hydroxycholest*-4-*eno*[3,4-b][1,4]*oxathian* 4′-*oxide* (XXI) as needles, (115 mg, 9·3%), m.p. 161—162° (from aqueous acetone) (Found: C, 69·8; H, 9·5; S, 6·05. $C_{31}H_{50}O_5S$ requires C, 69·85; H, 9·35; S, 6·0%), $[\alpha]_D^{16}$ −31·2° (*c* 0·94), $\lambda_{max.}$ 207 nm (ε 16,000), $\nu_{max.}$ 3230s (OH), 1735s, 1240s (CO_2Me), 1615w (C=C), and 1070s cm^{-1} [·S(O)·], τ 3·94 (1H, m, 6-H), 4·75—5·30 (1H, m, ·S·CH_2·CH_AH_B·O·) 5·95—6·30 (1H, m, ·S·CH_2·CH_AH_B·O·), 6·55—6·95 (2H, m, ·S·CH_2), 7·99 (3H, s, CO_2Me), 8·85 (3H, s, 19-H_3), and 9·25 (3H, s, 18-H_3), *m/e* 534·337 ($C_{31}H_{50}O_5S$) (M^+).

Further elution with benzene–ether (480 ml, 4 : 1) gave 6β-*acetoxy*-4-(2-*hydroxyethylthio*)*cholest*-4-*en*-3-*one* (XXII) as needles (270 mg, 23·0%), m.p. 122·5—123° (from aqueous methanol) (Found: C, 71·85; H, 9·75; S, 6·4. $C_{31}H_{50}O_4S$ requires C, 71·8; H, 9·75; S, 6·15%), $[\alpha]_D^{16}$ +43·5° (*c* 1·10), $\lambda_{max.}$ 247 (ε 8500) and 321 nm (1500), $\nu_{max.}$ 3440s (OH), 1735s, 1240s (CO_2Me), 1689s, and 1550w cm^{-1} [·CO·C(·S·):C·], τ 3·17 (1H, m, 6-H), 6·30—6·55 (2H, m, ·O·CH_2·CH_2·S·), 7·06—7·16 (2H, m, ·S·CH_2·CH_2·O·), 7·96 (3H, s, CO_2Me), 8·66 (3H, s, 19-H_3), and 9·25 (3H, s, 18-H_3), *m/e* 518·345 ($C_{31}H_{51}O_4S$) (M^+).

Further elution with benzene–ether (180 ml, 3 : 1) gave the enone (V) (79 mg, 7·3%), m.p. and mixed m.p. 163—183° (from light petroleum–ether).

The acidic products, obtained as an oil (37 mg), were not investigated further.

Desulphurization of the Ethoxy-enone (XVII) *with Raney Nickel.*—Treatment of the ethoxy-enone (XVII) (140 mg) with deactivated Raney nickel (*ca.* 4·2 g) in acetone (30 ml), and work-up as described for the enone (V) gave 6β-ethoxycholest-4-en-3-one (XVIII) (73 mg, 61·4%), m.p. and mixed m.p.[13] 112·5—113° (from methanol), identical with an authentic sample,[13] $\lambda_{max.}$ 237 nm (ε 13,700), $\nu_{max.}$ 1692s and 1620w cm^{-1} (CO·C:C).

Oxidation of the Ethoxy-enone (XVII).—(i) *With* m-*chloroperbenzoic acid.* Treatment of the ethoxy-enone (XVII) (430 mg) with *m*-chloroperbenzoic acid (200 mg) in dichloromethane (43 ml) and work-up as described for the oxathiin (I) gave the oxathian 4′-oxide (XIX) (195 mg, 44·0%), m.p. and mixed m.p. 123—124° (from aqueous acetone).

(ii) *With peracetic acid.* Treatment of the ethoxy-enone (XVII) (235 mg) with aqueous 30% hydrogen peroxide (0·11 ml) in acetic acid (2 ml) and work-up as described for the oxathiin (I) gave the same 4′-oxide (XIX) (86 mg, 35·5%).

Desulphurization of the Oxathian 4′-Oxide (XIX) *with Raney Nickel.*—Treatment of the 4′-oxide (XIX) (100 mg) with deactivated Raney nickel (*ca.* 2·1 g) in acetone (30 ml) and work-up as described for the enone (V) gave the ketone (XVIII), as needles (41 mg, 48·0%), m.p. and mixed m.p. 112—112·5° (from methanol).

Alkaline Hydrolysis of the Oxathian 4′-Oxide (XIX).—The oxide (XIX) (130 mg) was dissolved in 10% potassium hydroxide–absolute alcohol (13 ml), and the solution was kept at room temperature for 1·5 h and poured into ice–water (50 ml); the product was extracted into ether. The extract was washed with aqueous 10% hydrochloric acid and water, then dried (Na_2SO_4). On removal of the solvent *in vacuo* pale yellow crystals were deposited (128 mg), m.p. 92—98°, which were chromatographed over silica gel (13 g) with benzene–ether (50 ml, 9 : 1) as eluant to give cholest-4-ene-3,6-dione (XX) as pale yellow leaflets (56 mg, 56·3%), m.p. and mixed m.p.[8] 125—126° (from methanol), identical with an authentic specimen,[8] $\lambda_{max.}$ 253 nm (ε 11,700), $\nu_{max.}$ 3050w (HC:C), 1680s, and 1602m cm^{-1} (CO·C:C·CO·).

Acetylation of the Acetoxy-enone (XXII).—The hydroxy-compound (XXII) (33 mg) was dissolved in acetic anhydride–pyridine (0·8 ml, 1 : 1), and the solution was kept at room temperature for 3 h, then poured into ice–water (20 ml); the product was extracted into ether. The extract was washed with aqueous sat. sodium hydrogen carbonate and water, and then dried (Na_2SO_4). Removal of the solvent *in vacuo* gave an oily residue (35 mg), which was chromatographed over silica gel (3·5 g) with benzene (27 ml) to give the acetate (X) as an homogeneous (t.l.c.) oil (28 mg, 78·5%), which, on addition of methanol, crystallized as needles (21 mg, 58·9%), m.p. and mixed m.p. 63—64·5° (from methanol).

Oxidation of the Acetoxy-enone (XXII) *with* m-*Chloroperbenzoic Acid.*—Treatment of the enone (XXII) (100 mg) with *m*-chloroperbenzoic acid (70 mg) in dichloromethane (10 ml) and work-up as described for the oxathiin (I) gave the oxathian 4′-oxide (XXI) (59 mg, 57·2%), m.p. and mixed m.p. 160—162° (from aqueous acetone).

Desulphurization of the Oxathian 4′-Oxide (XXI) *by Raney Nickel.*—Treatment of the oxide (XXI) (140 mg) with deactivated Raney nickel (*ca.* 2·8 g) in acetone (30 ml) and work-up as before for the enone (V) gave cholest-5-en-3-one (XXIII) as needles (41 mg, 40·7%), m.p. and mixed m.p.[15] 124—127° (from ether–methanol), identical with an authentic specimen,[15] $\nu_{max.}$ 3035s (HC:C) and 1720s cm^{-1} (CO).

Desulphurization of the Hydroxy-enone (XXII) *with Raney Nickel.*—Treatment of the enone (XXII) (150 mg) as before with the enone (V) gave the ketone (XXIII) (40 mg,

35·9%), m.p. and mixed m.p. 123—126° (from ether–methanol), and cholest-4-en-3-one (XXIV) as needles (17 mg, 15·2%), m.p. and mixed m.p.[15] 79·5—81·5° (from methanol), identical with an authentic specimen,[15] $\lambda_{max.}$ 243 nm (ε 16,500), $\nu_{max.}$ 1682s and 1622m cm^{-1} (CO·C:C).

Ozonolysis of Cholesta-3,5-diene (XXV).—Ozonolysis of the diene (XXV) (200 mg) in chloroform–ethyl acetate–acetic acid (25 ml, 2 : 2 : 1) between −18 and −20° as before gave an oily residue (202 mg) as a neutral product. The oil showed nine poorly separated spots on t.l.c. (silica gel).

The acidic products, obtained as an oil (33 mg), were not further investigated.

Ozonolysis of 3-Ethoxycholesta-3,5-diene (XXVI).—Ozonolysis of the ethoxy-diene (XXVI) (1·2 g) in chloroform–absolute alcohol (30 ml, 4 : 1) at −20° was carried out as described for the oxathiin (I), giving crystals (1·210 g), m.p. 121—150°, as the crude neutral product. This material was chromatographed over silica gel (120 g), from which elution with benzene–ether (360 ml, 4 : 1) gave the hydroxy-enone (XI) (386 mg, 33·1%), m.p. and mixed m.p. 194·5—195·5° (from methanol).

Elution with benzene–ether (300 ml, 1 : 4) gave *6α-hydroxycholest-4-en-3-one* (XXVII) as needles (219 mg, 18·8%), m.p. 163·5—164° (from methanol) (Found: C, 80·75; H, 11·0. $C_{27}H_{44}O_2$ requires C, 80·95; H, 11·05%), $[\alpha]_D^{14}$ +80·0° (*c* 1·00), $\lambda_{max.}$ 243 nm (ε 14,700), $\nu_{max.}$ 3335s (OH), 1665s, and 1617m cm^{-1} (CO·CH:C), τ 3·85 (1H, d, *J* 1·2 Hz, 4-H), 5·70 (1H, m, 6-H), 8·82 (3H, s, 19-H_3), 9·28 (3H, s, 18-H_3), *m/e* 400·331 ($C_{27}H_{44}O_2$) (M^+).

The acidic products, as an oil (29 mg), were not investigated further.

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