4-THIA-5-CHOLESTEN-3-ONE AND SOME FURTHER STEROIDAL δ-THIOENOL LACTONES*

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δ-Oxo acids *VI*—*IX* and *XIV* were converted to δ-thiocnol lactones *X*—*XIII* and *XV* on reaction with phosphorus pentasulfide in pyridine. Under these conditions the ε-oxo acid *XVI* affords B-nor-steroids *XVII* and *XVIII*. The proposed structures are confirmed by a number of physico-chemical data. The reduction of these thienol lactones with hydrides is also described.

Among the modified steroids containing a sulfur atom in their nucleus only substances *I* and *II* have displayed a promising biological activity[1,2] so far. Among 4-thia-steroids only compounds of type *III* are known[3] which were prepared from cholesterol in 9 steps, but which do not represent a type in which hormonal activity could be expected. Therefore we described in this paper a one-step conversion of 5-oxo-A-nor-3,5-secocholestan-3-oic acid (*VI*) into 4-thia-5-cholesten-3-one (*X*), which we considered a model of substances with a potential biological activity.

The closing of a heterocycle when aliphatic oxo acids are used as starting substances usually takes place in low yields, especially with δ-oxo acids[4–6]. However, in the case of oxo acid *VI* the expectation of a successful cyclization to compound *X* was supported by the easy formation[7,8] of analogous 4-heterosteroids *IV* and *V*. For the transformation proper we chose the conditions which Barton and coworkers[9] used for the preparation of steroid thiones. Under these conditions compound *VI* gave a more lipophilic product *X* of the composition $C_{26}H_{42}OS$ (mass spectroscopy). The formation of compound *X* was accompanied by a strong shift of the molecular rotation to the left ($[M]_D^{20} = -350°$), the same as in the case of the formation of analogous substances *IV* and *V* ($[M]_D^{20} = -197°$ and $-297°$, respectively).

The IR spectrum of compound *X* contains a strong band at 1 668 cm^{-1} (ν(C=O)) and a weaker one at 1 635 cm^{-1} (ν(C=C)). The occurrence of the first of these bands, the frequency of which coincides with that of saturated tetrahydrothiapyran-2-ones[10], excludes — for compound *X* — the alternative structure of thionoenol lactone. In the UV region the conjugation of the thiol ester system with a double bond is apparent:

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while saturated tetrahydrothiapyran-2-ones absorb at 235 and 270 nm, compound *X* absorbs at 223, 238 and 258 nm. The CD-curve of compound *X* (Fig. 1) has the same course as the curves of analogous substances *IV* and *V*, but the frequencies of individual transitions differ in dependence on the length of the π-electron systems. In contrast to saturated thiepan-2-ones[11], the CD curves of compound *X* are practically identical (with the exception of the fine structure), irrelevant of whether they were measured in methanol, dioxane or heptane.

The ^{1}H NMR spectrum of compound *X* is almost identical with the spectra of compounds *IV* and *V*, with the exception of the larger downfield shift of the protons in the position 6 and 19. The ^{13}C NMR spectrum of compound *X* is again very similar to the spectra of the mentioned analogues (Table I), and in the case of the thia derivative *X* the conjugation of the free electron pairs of the sulfur atom with the π-electrons of the carbonyl group and the C=C bond is more pronounced, so that the most important deviations from the spectra of compounds *IV* and *V* consist in the chemical shifts of the signals of atoms $C_{(3)}$, $C_{(5)}$ and $C_{(6)}$. The signals of atoms vicinal to this conjugated system ($C_{(2)}$, $C_{(7)}$) are distinctly shifted downfield. With increasing distance of other atoms from this system the differences of the chemical shifts of the thia and oxa derivatives *X* and *V* disappear (see Table II).

In contrast to oxa- and aza-analogues *IV* and *V* the thia derivative *X* gives a well defined polarographic wave at an accessible potential ($\pi_{1,2} = -1{\cdot}75$ V). This wave is connected with the reduction of the carbonyl group, as evidenced by the absence of this wave in the experiment on polarographic determination of 3α-hydroxy--4-thia-5-cholestene (*XIXb*).

The utilisability of the preparation of Δ^5-unsaturated 4-thiasteroids of type *X* was checked on further substrates which contained an ester (*VII*) or a keto group

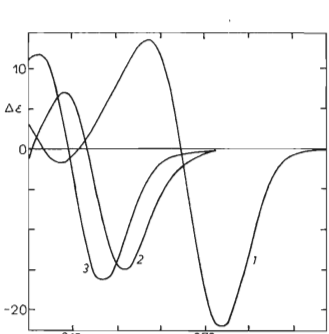
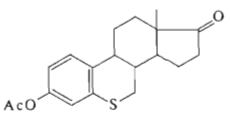


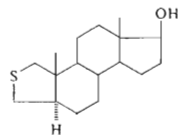
FIG. 1

CD spectra of *IV*, *V* and *X* in methanol. *1* Thia derivative *X*, *2* aza derivative *V*, *3* oxa derivative *IV*; $c = 1 \cdot 10^{-5}$ mol l^{-1}

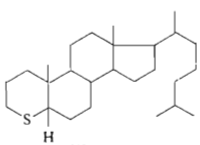
(*VIII*, *IX*) in the molecule. The physico-chemical characteristics of products *XI* – *XIII* confirmed that the formation of δ-thienol lactones took place without complications. Compounds with free hydroxyl groups which undergo dehydration under the reaction conditions are not suitable as substrates.



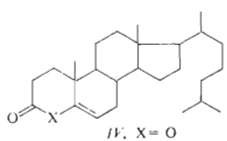
I



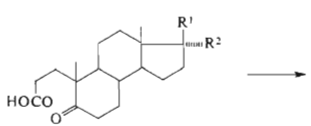
II



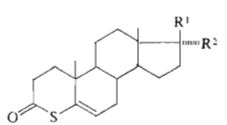
III



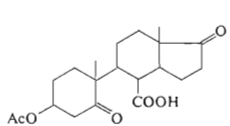
IV, X = O
V, X = NH



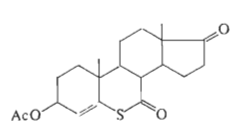
VI, $R^1 = i\text{-}C_8H_{17}$, $R^2 = H$
VII, $R^1 = OCOC_6H_5$, $R^2 = H$
VIII, $R^1 = COCH_3$, $R^2 = H$
IX, $R^1 + R^2 = O$



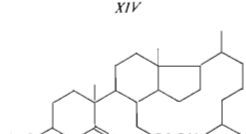
X, $R^1 = i\text{-}C_8H_{17}$, $R^2 = H$
XI, $R^1 = OCOC_6H_5$, $R^2 = H$
XII, $R^1 = COCH_3$, $R^2 = H$
XIII, $R^1 + R^2 = O$



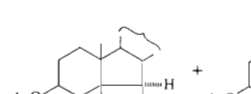
XIV



XV



XVI



XVII *XVIII*

This method was also applied to 3β-acetoxy-5,17-dioxo-B-nor-5,6-secoandrostan--6-oic acid (*XIV*) which gave 3β-acetoxy-6-thia-4-androstene-7,17-dione (*XV*) in low yield. On the other hand, the ε-oxo acid *XVI* gives under the same condition merely sulfur-free products; two main lipophilic products have been identified as B-norsteroids *XVII* and *XVIII* on the basis of their IR spectra which were identical with those of authentic samples.

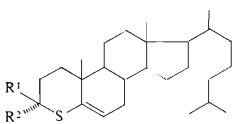
Thioenol lactones of type *X* easily undergo reduction. While enol lactone *IV* gets reduced with tri-tert-butoxylithium aluminium hydride under rearrangement[12] to 3,6-cyclo-A-nor-3,5-seco derivative *XX*, the reduction of thia derivative *X* with this reagent takes place without rearrangement: the product *XIX* contains a single oxygen-containing function in the molecule (mass and IR spectroscopy), *i.e.* a hydroxyl group, and the Δ^5-double bond remains preserved (^{1}H NMR). The character of the signal of the $C_{(3)}$-proton (a multiplet, $W_{1/2} = 8$ Hz) corresponds to a configuration in which this proton is coupled to the same extent with both protons on carbon $C_{(2)}$; if assuming a chair conformation for the A-ring[13], the reduction product should be expressed by formula *XIXb* in which the hydroxyl group is bound with an axial bond. In alcoholic medium substances of the type *XIXb*, *i.e.* derivatives with a masked aldehyde group, react to 3α-alkoxy derivatives of type *XIXc*. The

TABLE I

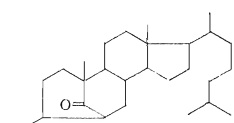
Parameters of the ^{13}C NMR spectra. The noise decoupled spectra were measured on a Varian XL 200 instrument in deuteriochloroform with tetramethylsilane as internal reference. Chemical shifts are given in δ-scale (ppm).

Carbon atom	Compound			Carbon atom	Compound		
	X	*IV*	*V*		*X*	*IV*	*V*
1	32·36	27·62	28·41	15	23·82	23·81	23·82
2	38·20	31·01	31·51	16	28·19	28·13	28·16
3	201·46	168·49	169·85	17	56·07	56·05	56·09
5	136·73	151·36	139·91	18	11·96	11·91	11·92
6	126·13	105·54	103·63	19	19·74	18·62	18·68
7	36·92	29·17	29·69	20	35·74	35·72	36·75
8	31·66	31·67	31·62	21	18·68	18·89	18·68
9	48·08	48·74	47·98	22	36·12	36·14	35·14
10	36·12	34·61	34·10	23	24·13	24·15	24·15
11	21·68	20·97	20·92	24	39·50	39·48	39·46
12	39·51	39·29	39·46	25	28·01	27·99	27·98
13	42·43	42·44	42·41	26	22·81	22·79	22·79
14	56·48	56·21	56·48	27	22·56	22·55	22·54

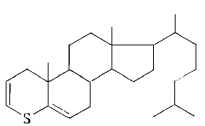
hydroxy group in compound *XIXb* is relatively easily split off, affording the conjugated system of 4-thia-2,5-cholestadiene, when submitted to acetylation, oxidation with dimethyl sulfoxide and oxalyl chloride, or prolonged standing at room temperature. Oxidation of hydroxy derivative *XIXb* according to Jones affords compound *XXII* in which the hydroxy group is preserved, but the sulfide bridge oxidized to a sulfone group (IR spectrum: intramolecular hydrogen bond from the hydroxyl group, sulfone group). In 3-oxo derivative *X* a similar oxidation of the sulfide bridge does not take place, but on prolonged reaction with Jones's reagent the A-ring is opened under formation of a carboxylic acid (IR spectrum).



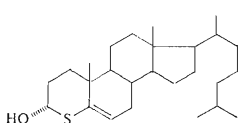
XIXa, $R^1 = OH$, $R^2 = H$
XIXb, $R^1 = H$, $R^2 = OH$
XIXc, $R^1 = H$, $R^2 = OCH_3$



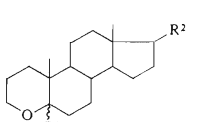
XX



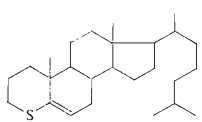
XXI



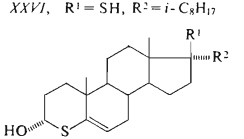
XXII



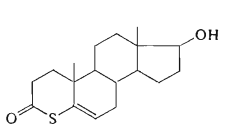
XXIII, $R^1 = H$, $R^2 = i\text{-}C_8H_{17}$
XXIV, $R^1 = C_6H_5CH_2$, $R^2 = OH$
XXVI, $R^1 = SH$, $R^2 = i\text{-}C_8H_{17}$



XXV



XXVII, $R^1 = C_6H_5COO$, $R^2 = H$
XXVIII, $R^1 + R^2 = O$
XXIX, $R^1 = OH$, $R^2 = H$



XXX

When the δ-thienol lactone *X* was reduced with lithium aluminium hydride and worked up using acids, the substance *XXIII* isolated was free of sulfur. The IR and the ^{1}H NMR spectra confirmed the identity with 3-hydroxy-A-nor-3,5-secocholestan-5-one which is present in solution[14,15] in cyclic form. Similar reduction of 17β--benzoyloxy derivative *XI* afforded alcohol *XXIV*. In reduction with lithium aluminium hydride the reaction does not come to a stop at the stage of hydroxy derivative *XIX*, but it continues up to 3-deoxy derivative of type *XXV* which reacts during the work-up procedure with the acidified water, giving gradually 3-hydroxy-5-thione *XXVI* and 3-hydroxy-5-ketone *XXIII*. The easy reducibility of the carbonyl group in δ-thienol lactones of type *X* is demonstatrated by the attempt at partial reduction of 4-thia-5-androstene-3,17-dione (*XIII*): the distribution of the products *XXVIII* to *XXX*, when less than one equivalent of tri-tert-butoxylithium aluminium hydride was used, shows that the 3-oxo group in compound *XI* is reduced roughly equally easily as the 17-keto group.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Optical rotations were measured in chloroform, the IR spectra in tetrachloromethane, unless stated otherwise. The ^{1}H NMR spectra were measured on a Tesla 60, and the ^{13}C NMR spectra on a Varian XL 200 instrument, in deuteriochloroform. The chemical shifts (in ppm) are given in δ-scale. The mass spectra were measured on an AEI MS 902 spectrometer, and circular dichroism on Dichrograph II (Jouan-Roussel) in methanol. Polarographic determinations were carried out in tetra-n-butylammonium perchlorate in dimethylformamide (0·1 mol l^{-1}), using Ag/AgCl electrode as a standard.

4-*Oxa*-5-*cholesten*-3-*one* (IV): ^{1}H NMR spectrum: 0·70 (s, 3 H, 18-H), 1·09 (s, 3 H, 19-H), 2·60 (mt, 2 H, 2-H), 5·27 (dd, J = 5 and 2 Hz, 1 H, 6-H) ppm.

4-*Aza*-5-*cholesten*-3-*one* (V): ^{1}H NMR spectrum: 0·70 (s, 3 H, 18-H), 1·09 (s, 3 H, 19-H), 2·47 (mt, 2 H, 2-H), 4·86 (mt, $W_{1/2}$ = 8 Hz, 1 H, 6-H) ppm.

4-Thia-5-cholesten-3-one (*X*)

Phosphorus pentasulfide (15 g) was added over one minute at 90°C and under stirring to a solution of 12 g of keto acid *VI* in 80 ml of pyridine and the mixture was stirred at the same temperature for 2 h. After cooling ether (250 ml) was added and the mixture was filtered through a layer of sodium sulfate, which was then washed with ether. The filtrate was concentrated in a vacuum, dissolved in about 100 ml of toluene and the solution was diluted with about 200 ml of ether. The mixture was filtered again through a layer of sodium sulfate, the filtrate was concentrated and applied on a silica gel column. Elution with 1% of ether in light petroleum gave 5·52 g of *X*, which crystallized from light petroleum at −60°C. However, at room temperature this substance turns oily and on standing crystallizes again. M.p. 60−63°C, $[\alpha]_D^{20}$ −87° (*c* 1·1); IR spectrum: 1 679 (—COS—), 3 020, 1 635 (C=C) cm^{-1}. IR spectrum ($CHCl_3$): 1 667, 1 109 (—COS—), 1 635 (C=C) cm^{-1}. UV spectrum (methanol), ε_{max} (λ): 4 210 (258 nm), 2 860 (238 nm), 5 800 (233 nm). ^{1}H NMR spectrum: 0·72 (s, 3 H, 18-H), 1·20 (s, 3 H, 19-H), 2·60 (mt, 2 H, 2-H), and 5·70 (dd, J = 5 and 2 Hz, 1 H, 6-H) ppm, CD-spectrum: Δε = 14·17 (250 nm) and −21·65 (283 nm).

For $C_{26}H_{42}OS$ (402·7) calculated: 77·55% C, 10·51% H, 7·96% S; found: 77·32% C, 10·63% H, 7·67% S.

17β-Benzoyloxy-4-thia-5-androsten-3-one (*XI*)

Similarly, the keto acid *VII* (600 mg) was converted to compound *XI* (210 mg), using phosphorus pentasulfide (210 mg) in 7 ml of pyridine as reagent. M.p. of the product was 209—211°C (acetone, heptane), $[\alpha]_D^{20}$ −69° (*c* 1·0). IR spectrum ($CHCl_3$): 1 669 (—COS—), 1 710, 1 280 (C_6H_5COO) cm^{-1}. ^1H NMR spectrum: 0·98 (s, 3 H, 18-H), 1·24 (s, 3 H, 19-H), 4·88 (t, J = 8 Hz, 1 H, 17-H), 5·74 (dd, J = 5 and 2 Hz, 1 H, 6-H), 7·47 and 8·03 (mt, 5 H, arom.) ppm. For $C_{25}H_{30}O_2S$ (410·7) calculated: 73·13% C, 7·37% H, 7·81% S; found: 73·14% C, 7·55% H, 7·83% S.

4-Thia-5-pregnene-3,20-dione (*XII*)

In a similar manner the oxo acid *VIII* (710 mg) was converted to thioenol lactone *XII* (196 mg), m.p. 172—174°C (acetone, heptane) $[\alpha]_D^{20}$ −90° (*c* 0·9). IR spectrum ($CHCl_3$): 1 669 (COS), 1 637 (C=C), 1 700 and 1 360 ($COOH_3$) cm^{-1}. ^1H NMR spectrum: 0·67 (s, 3 H, 18-H), 1·20 (s, 3 H, 19-H), 2·11 (s, 3 H, 21-H), 2·55 (mt, 2 H, 2-H), 5·70 (bd, J = 5 Hz, 1 H, 6-H) ppm. For $C_{20}H_{28}O_2S$ (344·5) calculated: 73·21% C, 8·19% H, 9·31% S; found: 73·04 C, 8·10% H, 8·96% S.

17-Oxo-4-thia-5-androsten-3-one (*XIII*)

Similarly acid *IX* (2·6 g) was converted on reaction with phosphorus pentasulfide (2·3 g) in pyridine (40 ml) at 90°C to compound *XIII* (680 mg), m.p. 156—158°C (ether), 162—163°C (aqueous acetone), $[\alpha]_D^{20}$ −124° (*c* 2). IR spectrum ($CHCl_3$): 1 745 (CO), 1 682 (—COS—), 3 035, 1 638 (C=C) cm^{-1}. ^1H NMR spectrum: 0·92 (s, 3 H, 18-H), 1·24 (s, 3 H, 19-H), 2·63 (mt, 2 H, 2-H), 5·75 (dd, J = 2·2 and 5 Hz, 1 H, 6-H) ppm. For $C_{18}H_{24}O_2S$ (304·4) calculated: 71·01% C, 7·95% H; found: 69·93%C , 7·88% H.

3β-Acetoxy-6-thia-4-androstene-7,17-dione (*XV*)

In a similar manner diketo acid *XIV* (2·5 g) was converted to compound *XV* (0·45 g) on reaction with 3·9 g of phosphorus pentasulfide in 25 ml of pyridine. M.p. 191—193°C (acetone), $[\alpha]_D^{20}$ +163° (*c* 1·1). IR spectrum ($CHCl_3$): 1 732, 1 250 (CH_3COO), 1 740 (CO, ketone), 1 670, 1 625 (—COS—) cm^{-1}. CD spectrum: $\Delta\varepsilon$ = +19·41 (287 nm), 0 (263 nm), −6·71 (253 nm), −4·38 (237 nm), −5·25 (228 nm), −3·94 (217 nm). ^1H NMR spectrum: 0·90 (s, 3 H, 18-H), 1·27 (s, 3 H, 19-H), 2·03 (s, 3 H, CH_3CO), 5·30 (mt, $W_{1/2}$ = 15 Hz, 1 H, 3-H), 5·52 (mt, $W_{1/2}$ = = 4 Hz, 1 H, 4-H) ppm. For $C_{20}H_{26}O_4S$ (362·5) calculated: 66·27% C, 7·23% H; found: 66·13% C, 7·36% H.

Reaction of 3β-Acetoxy-5-oxo-5,6-secocholestan-6-oic Acid (*XVI*) with Phosphorus Pentasulfide

Similarly, keto acid *XVI* (230 mg) was exposed to the action of phosphorus pentasulfide in pyridine, the product was separated on silica gel thin layer (with 10% ether in benzene) and the zones detected with a methanolic morin solution. The main product (68 mg) was found identical with the β-lactone *XVII*, IR spectrum in chloroform: 1 731, 1 256, 3 040, 1 820, 1 191 cm^{-1}, identical with the spectrum of an authentic sample[16]. The by-product (11 mg) was found identical with B-norcholesteryl acetate[16] (*XVIII*). In the region of non-polar substances no sulfur derivative was found.

4-Thia-5-cholesten-3α-ol (*XIXb*)

3-Oxo derivative *X* (220 mg) was dissolved in tetrahydrofuran (4 ml) and then mixed at room temperature with 400 mg of tri-tert-butoxylithium aluminium hydride. After 1 h reaction the mixture was poured into a saturated solution of sodium ammonium tartrate (about 100 ml) and the product was extracted with chloroform. The extract was washed with water and dried over sodium sulfate. Crystallization from acetone afforded 83 mg of compound *XIXb*, m.p. 112–120°C $[\alpha]_D^0$ −20° (*c* 1·0). IR spectrum: 3 065, 1 065, 1 025, 1 012 (OH), 3 025 (C=C), cm^{-1}. ^1H NMR spectrum: 0·68 (s, 3 H, 19-H), 0·86 (d, J = 6 Hz, 6 H, 26, 27-H), 0·91 (d, J = 6 Hz, 6 H, 3 H, 21-H), 4·88 (mt, $W_{1/2}$ = 7 Hz, 1 H, 3-H), 5·85 (bd, J = 5 Hz, 1 H, 6-H) ppm. For $C_{26}H_{44}OS$ (404·7) calculated: 77·16% C, 10·96% H; found: 76·91% C, 8·06% H.

4-Thia-androstene-3,17-diol, 17-benzoate (*XXVII*)

3-Oxo derivative *XI* (160 mg) was reduced at room temperature with sodium borohydride (300 mg) in tetrahydrofuran (2 ml). After 10 min the mixture was poured into 5% of hydrochloric acid, the product was extracted with chloroform, the extract washed with an aqueous potassium hydrogen carbonate solution, then water, and dried. The product was purified by thin-layer chromatography on silica gel (10% of ether in benzene). The main product (105 mg) was crystallized from acetone and heptane, m.p. 154–158°C; $[\alpha]_D^{20}$ +28° (*c* 1·2). IR spectrum: 3 610 (OH), 1 722, 1 276 (C_6H_5COO) cm^{-1}. ^1H NMR spectrum: 0·95 (s, 3 H, 18-H), 1·25 (s, 3 H, 19-H), 4·85 (mt, $W_{1/2}$ = 13 Hz, 2 H, 3,17-H), 5·85 (mt, $W_{1/2}$ = 13 Hz, 2 H, 3,17-H), 5·85 (mt, $W_{1/2}$ = = 8 Hz, 1 H, 6-H), 7·05 and 8·05 (mt, 5 H, arom) ppm. For $C_{25}H_{32}O_3S$ (412·6) calculated: 72·77% C, 7·82% H; found: 72·50% C, 7·96% H.

4-Oxa-5ξ-cholestan-5-ol (*XXIII*)

45 mg of 4-thiacholestenone were mixed with a saturated lithium aluminium hydride solution in ether (5 ml) at room temperature. After 20 h standing the solution was poured into a 5% hydrochloric acid solution, the product was extracted with ether, the extract washed with potassium hydrogen carbonate and water, and dried. After evaporation of the solvent the crude dry residue contained a substance of molecular weight 390, accompanied by an admixture with molecular weight 388, the composition of which corresponds to substance *XXV* (high resolution mass spectrometry: $C_{26}H_{44}S$). After thin-layer chromatography on silica gel 32 mg of a mixture of 4-oxa-5ξ-cholestan-5-ols (*XXIII*) the IR spectrum of which is identical with the spectrum of this mixture prepared by a different route[15].

5-Benzyloxy-4-oxa-5ξ-androstan-17β-ol (*XXIV*)

17β-Benzoyloxy-4-thia-5-androsten-3-one (520 mg) was reduced with lithium aluminium hydride in tetrahydrofuran at room temperature for 20 h. The excess of the reagent was decomposed with moist ether, then with water and the mixture was saturated with anhydrous sodium sulfate. The inorganic material was filtered off and washed with ether. The filtrate was evaporated and the residue, smelling of hydrogen sulfide, was purified by chomatography on a silica gel column, affording 280 mg of the main product, which was crystallized from acetone, m.p. 233–236°C (51 mg). Mass spectrum (*m/z*): 276 ($C_{25}H_{36}O_2$–C_7H_8O), 108 (C_7H_8O). ^1H NMR spectrum: 0·72 (s, 3 H, 18-H), 0·98 (s, 3 H, 19-H), 3·63 (mt, 2 H, 3- and 17-H), 4·43 (d, J = 6 Hz, 1·5 H, benzyl), 4·67 (s, 0·5 H, benzyl), 7·35 (s, 5 H, arom)., ppm. IR spectrum ($CHCl_3$): 3 615 (OH), 3 095, 3 075, 1 609, 1 499 (arom.), 1 136, 1 096, 1 080, 1 056 (and 1 019 (—O—) cm^{-1}. For $C_{25}H_{36}O_3$ (384·5) calculated: 78·08% C, 9·44% H; found: 78·23% C, 9·47% H.

4-Thia-2,5-cholestadiene (*XXI*)

From the mother liquors after crystallization of compound *XIXb* (100 mg) a non polar product was also obtained by thin-layer chromatography on silica gel. M.p. 91–92°C (3 mg), $[\alpha]_D^{20}$ −91° (*c* 1·1). IR spectrum: 1 635, 1 619, 3 050, 3 030, 657 (C=C) cm^{-1}; ^1H NMR spectrum (200 MHz): 0·70 (s, 3 H, 18-H), 1·12 (s, 3 H, 19-H), 0·86 (d, J = 6·6 Hz, 3 H, 27-H), 0·87 (d, J = 6·6 Hz, 3 H, 26-H), 0·92 (d, J = 6·5 Hz, 3 H, 21-H), 1·87 (bd, $J_{1,3}$ = 2·9 Hz, $J_{1\alpha,2}$ = 2·4 Hz, ^2J = = 17 Hz), 2·32 (bd, $J_{1\beta,2}$ = 6·5 Hz, ^2J = 17 Hz), 5·70 (mt, $J_{2,1\beta}$ = 6·5 Hz, $J_{2,3}$ = 10 Hz, $J_{2,1\alpha}$ = 2·4 Hz), 5·94 (dd, $J_{3,2}$ = 10 Hz, $J_{3,1\alpha}$ = 2·9 Hz), 5·70 (mt, J = 5·4 and 2·8 Hz) ppm. Mass spectrum: 386 m/z ($C_{26}H_{42}S$).

4-Thia-5-cholesten-3α-ol S,S-dioxide (*XXII*)

4-Thia-5-cholesten-3α-ol (*XIX*, 300 mg) was oxidized according to Jones in acetone at 0°C. After 3 min the mixture was decomposed with an aqueous potassium carbonate solution, the product was extracted with chloroform, the extract washed and then purified on a thin layer of silica gel (with 8% ether in benzene). The polar product (R_f 0·2) melted at 154–158°C (61 mg), when crystallized from heptane the melting point rose to 165–167°C, $[\alpha]_D^{20}$ −21° (*c* 0·9). IR spectrum ($CHCl_3$): 3 565 (OH), 3 035, 1 644 (C=C), 1 290, 1 124, 1 103 (SO_2) cm^{-1}. Mass spectrum (m/z): 436 ($C_{26}H_{44}O_3S$). ^1H NMR spectrum: 0·67 (s, 3 H, 18-H), 1·31 (s, 3 H, 19-H), 0·85 (d, J = Hz, 6 H, 26,27-H), 0·90 (d, J = 6 Hz, 3 H, 21-H), 4·58 (mt, $W_{1/2}$ = 7·5 Hz, 1 H, 3-H), 6·95 (mt, $W_{1/2}$ = 9 Hz, 1 H, 6-H). For $C_{26}H_{44}O_3S$ (436·7) calculated: 71·51% C, 10·16% H; found: 71·32% C, 10·26% H.

Reduction of 4-Thia-5-androstene-3,17-dione (*XIII*) with Tri-tert-butoxylithium Aluminum Hydride

Tri-tert-butoxylithium aluminium hydride (90 mg) was added to a solution of 93 mg of compound *XIII* in 1 ml of tetrahydrofuran at 0°C and under stirring. After 15 min the mixture was decomposed by pouring it into a saturated solution of sodium potassium sulfate and the product was extracted with chloroform. Chromatography of the extract on silica gel thin layers (with 50% ether in benzene, detection with morin) afforded the following products (in order of increasing polarity): Starting compound *XIII* (31 mg). 3α-Hydroxy-4-thia-5-androsten-17-one (*XXVIII*, 19 mg), m.p. 187–190°C (acetone), $[\alpha]_D^{20}$ +45° (*c* 0·8). IR spectrum ($CHCl_3$): 1 740 (cyclopentane system), 3 598 and 1 065 (OH) and 1 635 (C=C) cm^{-1}; mass spectrum: M^+ = 306m/z. 17β-Hydroxy--4-thia-5-androsten-3-one (*XXX*, 32 mg), b.p. 163–164·5°C (acetone), $[\alpha]_D^{20}$ −162° (*c* 0·8). IR spectrum ($CHCl_3$): 1 665 (C=O), 1 635 (C=C), 3 615, 1 075, 1 021 (OH) cm^{-1}. Mass spectrum: M^+ = 306m/z. 4-Thia-5-androstene-3α,17β-diol (*XXIX*, 8 mg), m.p. 178–181°C. IR spectrum ($CHCl_3$): 3 610, 1 020 (OH), 1 634 (C=C) cm^{-1}.

3α-Methoxy-4-thia-5-cholestene (*XIXc*)

Five drops of a hydrochloric acid (1 drop) solution in methanol (1 ml) were added to a solution of 60 mg of a mixture of hydroxy derivatives *XIXa* and *XIXb* in 5 ml of methanol and the mixture was allowed to stand for 3 h. It was then cooled and the crystallized product (42 mg) was filtered off under suction and washed with methanol. From the mother liquors a further product was obtained (10 mg). M.p. 104–109°C and then again at 115–116°C $[\alpha]_D^{20}$ +26° (*c* 0·9). IR spectrum: 2 830, 1 097 (OCH_3), 1 634 (C=C) cm^{-1}. ^1H NMR spectrum: 0·68 (s, 3 H, 18-H), 0·85 (d, J = Hz, 6 H, 26,27-H), 1·24 (s, 3 H, 19-H), 3·38 (s, 3 H, OCH_3), 4·28 (dd, J = 3 and 3 Hz, 1 H, 3-H), 5·82 (bd, J = 4 and 2·5 Hz, 6-H) ppm. For $C_{27}H_{46}OS$ (418·7) calculated: 77·45% C, 11·07% H; found: 77·28% C, 10·99% H.

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