UDC 547.92/.93

90. Ken'ichi Takeda, Taichiro Komeno, and Shoichi Ishihara : Bile Acids and Steroids. XXIII.[1,2] Thiosteroids. (8).[1] Intramolecular Condensation of Some 6-Acetylthio Steroids.

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Previously, we examined the epoxide ring opening of cholesterol with thiolacetic acid to introduce acetylthio group at position 6, and there was obtained 6β-acetylthiocholestane-3β,5α-diol 3-acetate (II)[3] by epoxide ring fission of I.

Now, we have carried out this reaction on the cyclic 3-ethyleneacetal-5-ene derivatives. When treated 3,3-ethylenedioxy-5α-cholestane 5α,6α-epoxide (III) with 5~6 mole of thiolacetic acid for about 60 hours at room temperature followed by acid hydrolysis, it gave 5α-hydroxy-6β-acetylthiocholestan-3-one (IV), m.p. 185~186°, UV λ_{max}^{EtOH} mμ (ε) : 234 (4720), 305 (230); IR ν_{max}^{Nujol} cm^{-1} : 3421, 1707, 1702, 1136, 1119; $[\alpha]_D^{30}$ −56.4° (chloroform), in about 90 % yield.

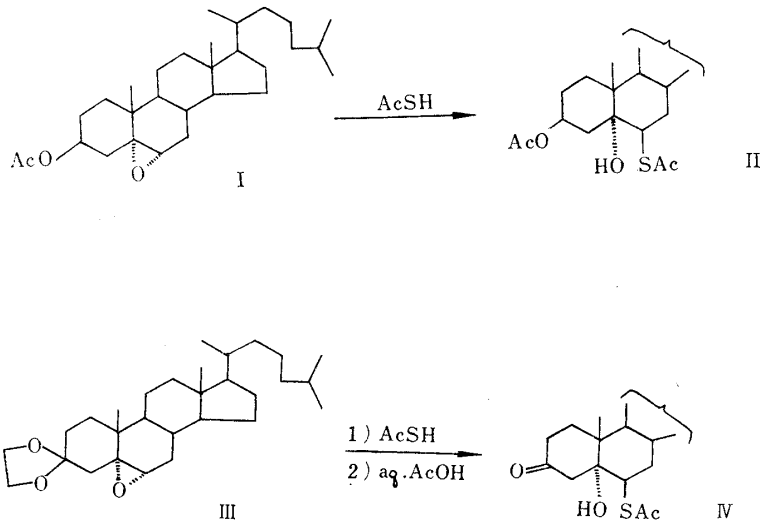

Chart 1.

IV was dehydrated with thionyl chloride in pyridine to the α,β-unsaturated ketone, $C_{29}H_{46}O_2S$ (V), m.p. 106~107°, UV : λ_{max}^{EtOH} 240 mμ (ε, 15320); IR ν_{max}^{Nujol} cm^{-1} : 1693, 1672, 1612, 1124; $[\alpha]_D^{29}$ +168.5° (chloroform). The infrared and the ultraviolet spectrum indicated the presence of an acetylthiol and an α,β-unsaturated ketone in the molecule. However, this compound showed strong *dextro* rotatory power and this result, as mentioned below, threw some doubt on the β-configuration of the 6-acetylthio group. In order to clarify this point the dehydration product was then treated with *p*-toluenesulfonic acid in acetic acid at room temperature for 2 days to epimerize the substituent at 6-position and there was obtained only an oily substance. Although an attempt to crystallize this substance through florisil chromatography was unsuccessful, the infrared and the ultraviolet spectrum of this substance also showed the presence of the α,β-unsaturated ketone and the acetylthio group, but were not identical with the optical data of the

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1) Part XXII (7) : K. Takeda, T. Komeno : This Bulletin, **10**, 1173 (1962).
2) This paper was read at the International Congress on Steroidal Hormones in Milan, Italy, May 15, 1962.
3) T. Komeno : This Bulletin, 8, 672 (1960).

above-mentioned compound V. On the other hand, when this oily residue of the florisil chromatography was rechromatographed through a basic alumina column, it gave a crystalline product VII having a melting point of 132°, UV : λ_{max}^{EtOH} mμ(ε) : 221 (12630), 269 (11470), 305 (2280); IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 1658, 1574, 1493; $[\alpha]_D^{29}$ −11° (chloroform); semicarbazone, $C_{30}H_{47}ON_3S$, m.p. 283~285° (decomp.). Analytical values of this compound VII are in good agreement with the formula $C_{29}H_{44}OS$, the dehydration product of V. Molecular weight determination of the analogous substance of the progesterone series was carried out and the result showed that intramolecular dehydration had occurred and not intermolecular dehydration. This compound underwent Huang-Minlon reduction and gave a *desoxo* derivative VIII, m.p. 96°, UV : λ_{max}^{EtOH} 246 mμ (ε 8870); Raman ν cm^{-1}, 1595~1600; $[\alpha]_D^{24}$ +17.9° (chloroform).

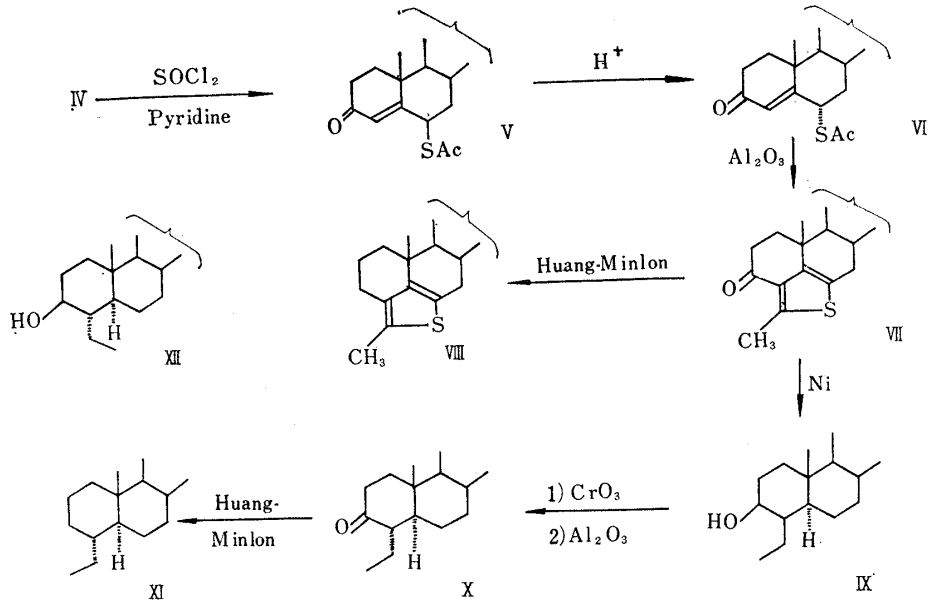


Chart 2.

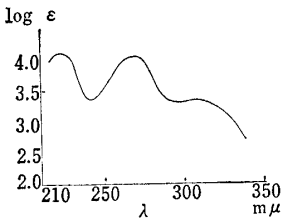


Fig. 1. Ultraviolet Spectrum of 5′-Methylthieno[4′,3′,2′-4,5,6]cholest-5-en-3-one (VII) in Ethanol

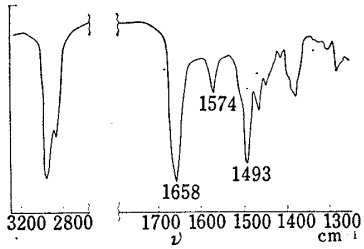


Fig. 2. Infrared Spectrum of 5′-Methylthieno[4′,3′,2′-4,5,6]cholest-5-en-3-one (VII) in Chloroform

To confirm the structure of this dehydration product, the Raney-Nickel desulfurization reaction was then examined. VII and the freshly prepared W-2 Raney-Nickel were refluxed in dioxane for 8 hours, and there was obtained an alcohol IX, $C_{29}H_{52}O$, m.p. 171°, IR $\nu_{max}^{CS_2}$ cm^{-1} : 3628, 1039, 997 (w); $[\alpha]_D^{29}$ +6.4° (chloroform), in 52% yield. This IX was then oxidized to a ketone X, $C_{29}H_{50}O$, m.p. 122°, IR : ν_{max}^{Nujol} 1712 cm^{-1}; $[\alpha]_D^{21}$ +38.3° (chloroform), with chromium trioxide in acetic acid and purified by alumina chromatography. The rotatory dispersion curve of this ketone in methanol*[2] showed a positive

*[2] The rotatory dispersion curves of this compound were kindly measured by Dr. C. Djerassi (Stanford University).

Cotton effect and furthermore this curve was not affected by the addition of hydrochloric acid to the solvent (see Fig. 3). It is then assumed that this compound is a cholestan-3-one derivative having an equatorial alkyl substituent at position 2 or 4.[4] Huang-Minlon reduction of this ketone gave a carbonhydrate XI, $C_{29}H_{52}$, m.p. 88°, $[\alpha]_D^{24}$ +10.9° (chloroform), corresponding to ethyl cholestane. Melting points and $[\alpha]_D$ values of the ketone X and the carbonhydrate XI derived from the acetylthiocholestenone are respectively in good agreement with those of the corresponding 4α-ethylcholestan-3-one and 4α-ethylcholestane.[5,6] The latter two compounds were synthesized from cholest-4-en-3-one by ethylation with ethyl iodide in potassium *t*-butoxide followed by lithium-liq. ammonia reduction gave X, and XI was also obtained by its Huang-Minlon reduction. These two compounds are identical with those derived from the acetylthio derivative in all respects.

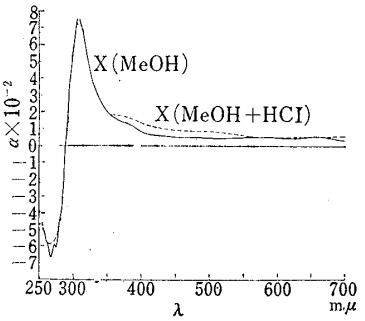


Fig. 3. Rotatory Dispersion Curves of 4α-Ethylcholestan-3-one (X) in Methanol and in Methanol-Hydrochloric Acid

From these results it was deduced that the oxygen atom of the acetylthio group was concerned with the dehydration reaction by basic alumina and that the structure of the finally obtained product is represented by the formula VII, a thiophene derivative.

This structure was also supported by the optical data. The bands at 1574 and 1493 cm^{-1} in the infrared spectrum of VII and the relative intensity of the latter to the former (ca. 2:1) are coincide well with the results of some acetylthiophene derivatives obtained by Yamaguchi.[7]

The presence of a maximum at 269 mμ of VII and a maximum at 246 mμ of its Huang-Minlon reduction product VIII corresponded well to the maximum at 250 mμ of β-acetylthiophene and at 231 mμ of thiophene in the ultraviolet spectrum, reported by Gronowitz.[8] No characteristic absorption band corresponding to the aromatic ring appeared in the infrared spectrum but a weak absorption band was observed at about 1595~1600 cm^{-1} in the Raman spectrum of VIII. The proton signal corresponding to the methyl group attached on the aromatic thiophene ring in VIII was observed at τ=7.28, but no olefinic proton in the nuclear magnetic resonance spectrum.

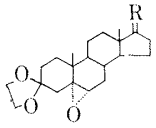
Although the physical constants of the alcohol IX obtained by desulfurization of VII differed markedly from the corresponding constants of 4α-ethylcholestan-3β-ol (XII), m.p. 143° or 147°, IR : $\nu_{max}^{CS_2}$ 1034 cm^{-1}, $[\alpha]_D$ +24° or 28°, reported by Djerassi[5] and Brown,[6] its structure is assumed as one of the isomers of 4-ethylcholestan-3-ol. Djerassi *et al.*[9] reported that cholestan-3-one was reduced to the equatorial 3β-ol in 83 % yield by freshly prepared W-2 Raney-Nickel in refluxing absolute ethanol. Furthermore, it was

4) C. Djerassi : "Optical Rotatory Dispersion" (McGraw-Hill), 145 (1960).
5) C. Djerassi, M. Cais, L. A. Mitscher : J. Am. Chem. Soc., **80**, 247 (1958).
6) B. R. Brown, P. W. Trown, J. M. Woodhouse : J. Chem. Soc., **1961**, 2478.
7) M. Yamaguchi : Anal. Chem. (Japan), **7**, 210 (1958).
8) S. Gronowitz : Arkiv. Kemi., **13**, 239 (1959).
9) C. Djerassi, A. J. Manson, M. Gorman : J. Am. Chem. Soc., **77**, 4925 (1955).

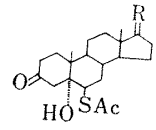
reported by Cole[10] and Allsop[11] that when the steroids have a 3-equatorial alcohol either with or without a gem-substituent at position 4, C-O streching absorption band of these compounds appears between 1020~1040 cm^{-1} in the infrared spectra. The absorption band at 1039 cm^{-1} of IX coincides with the results obtained by them. From these facts, the structure of the alcohol IX was assumed as 4β-ethylcholestan-3β-ol, and its oxidation product, 4β-ethylcholestan-3-one, was epimerized to the equatorial 4α-ethyl derivative during the purification of the crude ketone by alumina chromatography. This is also reasonable in the desulfurization reaction, since the chemisorption of Nickel occurred from the back side of the steroidal molecule, desulfurization and reduction from the α-side were induced simultaneously, thus 4β-ethylcholestan-3β-ol (IX) was obtained.

The above-mentioned intramolecular condensation reaction of the 6-acetylthio-Δ^4-3-one group was also applied to progesterone, or testosterone and its derivative, and in each case it gave a thiophene derivative, analogous to VII. The physical constants of those intermediates are cited in Table I.

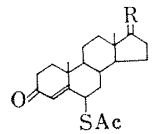
Table I.



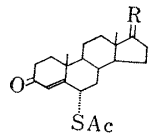
	IIIa	IIIb	IIIc
R =	α-H,β-C$(OCH_2)_2\cdot CH_3$	α-H,β-OAc	$(OCH_2)_2$
m.p., $[\alpha]_D$	186~187°, −48°	180~181°, −69°	212~214°, −84°



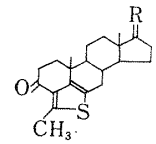
	IVa	IVb	IVc
R =	α-H,β-CO·CH_3	α-H,β-OAc	O
m.p., $[\alpha]_D$	227~229°, −27°	225~226°, −83°	238~240°, −14°
UV : λ_{max} mμ (ε)	234(5,890)	233.5(5,140)	234(5,010)
IR : ν_{max}^{Nujol} cm^{-1}	3234, 1706, 1691, 1677, 1122	3454, 1724, 1688, 1136	3366, 1739, 1707, 1137, 1114



	Va	Vb	Vc
R =	α-H,β-CO·CH_3	α-H,β-OAc	O
m.p., $[\alpha]_D$	185~187°, +243°	144~145°, +187°	170~171°, +299°
UV : λ_{max} mμ (ε)	238(15,140)	237(15,960)	237(15,820)
IR : ν_{max} cm^{-1}	1695, 1118, 1660, 1611 (Nujol)	1740, 1698, 1132, 1683, 1614 (CCl_4)	1737, 1689, 1117, 1678, 1617 ($CHCl_3$)



	VIa	VIb	VIc
R =	α-H,β-$COCH_3$	α-H,β-OAc	O
m.p., $[\alpha]_D$	no XI	192~194°, +40°	no XI
UV : λ_{max} mμ (ε)		235(16,820)	
IR : ν_{max} cm^{-1}		1741, 1687, 1618 (CCl_4)	1736, 1688(sh.), 1679, 1616, 1125($CHCl_3$)



	VIIa	VIIb	VIIc	VIId
R =	α-H,β-$COCH_3$	α-H,β-OAc	α-H,β-OH	O
m.p., $[\alpha]_D$	163~164°, +38°	147~148°, −33°	208~210°, −27°	234~235°, +39°
UV : λ_{max} mμ (ε)	221(13,480), 268(12,370), 302(2,670)	221 (12,900), 268.5(12,740), 304 (2,420)	221 (12,550), 268.5(11,740), 304 (2,360)	221 (13,730), 268.5(12,240), 304 (2,710)
IR : $\nu_{max}^{CHCl_3}$ cm^{-1}	1696, 1663, 1570, 1491	1726, 1664, 1575, 1495	3620, 3354, 1665, 1573, 1494	1735, 1664, 1573, 1493

Only in the case of the testosterone series, the epimerized product of the 6β-acetylthio-enone (Vb) with *p*-toluenesulfonic acid gave a crystalline product having a melting point of 192~194°.

10) A.R.H. Cole : J. Chem. Soc., **1952**, 4969; A.R.H. Cole, R.N. Jones, K. Dobriner : J. Am. Chem. Soc., **74**, 5571 (1952).

11) I.L. Allsop, A.R.H. Cole, D.E. White, R.L.S. Willix : J. Chem. Soc., **1956**, 4868.

6β-Acetylthiotestosterone acetate (Vb) also showed *dextro*-rotation, $[\alpha]_D^{24}$ +186.5° (chloroform), and the compound treated with *p*-toluenesulfonic acid (VIb) showed less *dextro*-rotatory power, $[\alpha]_D^{22.5}$ +40.3° (chloroform), and these results are inverted $[\alpha]_D$ values of the Δ^4-3-keto steroids having an epimeric substituent at the position 6 (cf. Table II). In other words, all the 6α-derivatives showed much more strong *dextro*-rotation than the 6β analogs.

But, when comparing the ultraviolet spectrum of Vb with that of VIb, the absorption maximum at 235 mμ of the latter shifted to the shorter wave length about 2 mμ from that of the former and its intensity was also increased in the latter. Analogous phenomena were also observed in the case of the 6-bromo, 6-chloro, 6-acetoxy substituted Δ^4-3-keto steroids as shown in Table II.*3

Table II. Ultraviolet and M_D Data of 6-Substituted-Δ^4-en-3-ones

	Compounds	UV : λ_{max} mμ (ε)	M_D	ΔM_D ($\beta-\alpha$)
1) Me[a]	6β-Methyltestosterone	242 (16, 200)	+181	−103
	6α-Methyltestosterone	242 (15, 150)	+284	
2) Br[b]	6β-Bromocholestenone	244 (13, 700)	+ 28	−182
	6α-Bromocholestenone	238 (15, 800)	+245	
3) Cl[b]	6β-Chlorocholestenone	241 (15, 100)	+ 65	−217
	6α-Chlorocholestenone	239 (19, 000)	+247	
4) F[c]	6α-Florotestosterone	234 (12, 300)	± 0	−312
	6α-Florotestosterone	237 (14, 450)	+312	
5) OH[b]	6β-Hydroxycholestenone	236 (13, 500)	+108	−216
	6α-Hydroxycholestenone	240 (16, 200)	+324	
6) OAc[b]	6β-Acetoxycholestenone	237 (12, 600)	+159	−177
	6α-Acetoxycholestenone	236 (16, 600)	+336	
7) SAc	6β-Acetylthiotestosterone acetate (Vb)	237 (15, 960)	+754	+591
	6α-Acetylthiotestosterone acetate (VIb)	235 (16, 820)	+163	

a) J. A. Campbell, J. C. Babcock, J. H. Hogg : J. Am. Chem. Soc., **80**, 4717 (1958).
b) C. W. Bird, R. C. Cookson, S. H. Dangegaonker : J. Chem. Soc., **1956**, 3675.
c) A. Bowers, H. J. Ringold : Tetrahedron, **3**, 14 (1958).

The optical rotatory dispersion curve of VIb showed a negative Cotton effect as in the case of 6α-methyltestosterone[12] and is essentially identical to that of an unsubstituted Δ^4-3-keto steroid. While in the case of Vb it showed a positive Cotton effect similar to that of the steroids having an axial substituent at the C-6 position, such as the 6β-methyl-, 6β-chloro- or 6β-bromo-testosterone derivative.[13]

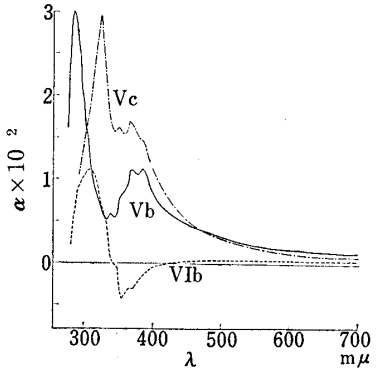


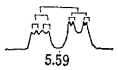
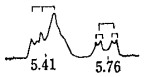
Fig. 4. Rotatory Dispersion Curves of 6β-Acetylthiotestosterone Acetate (Vb) 6α-Epimer (VIb), and 6β-Acetylthioandrost-4-en-3,17-dione (Vc) in Dioxane

*3 A detailed discussion on the K-bands of these derivatives was reported by H. J. Ringold, A. Bowers: Experientia, **17**, 65 (1961).
12) C. Djerassi : "Optical Rotatory Dispersion," 63 (1960).
13) *Idem* : *Ibid.*, 130 (1960).

These facts are in agreement with the assumption of the 6β-acetylthio group in Vb, in spite of the difference in the values of $[\alpha]_D$.

The nuclear magnetic resonance spectrum of the 6α-acetylthioandrost-4-ene-3,17-dione (VIc) showed an ABX type quartet of the proton signal of C-6 hydrogen at $\tau=5.59$ and each quartet was split into a doublet due to coupling with the 4-position proton. With this respect the proton signal of the C-4 position was observed at $\tau=4.0$ as a doublet ($J=1.7$ cps.). It indicates also that the hydrogen atom at C-6 in VIc is an axial one. Although VIc is an oily substance, we chose VIc as a model substance, because in the case of VIb the signals of the C-6 proton and those of the C-17 overlapped each other. But even in the latter case, it is also possible to identify the half of the quartet corresponding to the axial proton signal at position 6 in VIb.

Table III. Nuclear Magnetic Resonance Data of 6-Acetylthio Compounds
(τ-Values measured by Varian A-60)

Compd.	Solvent	4-H	6-H and/or 17α-H	CH_3 of SAc group	CH_3 of OAc group	19-H	Δ (p.p.m.)	18-H	Δ (p.p.m.)
Androst-4-ene-3,17-dione	$CHCl_3$	4.32 (s)				8.79		9.09	
6β-Acetylthioandrost-4-ene-3,17-dione (Vc)	$CHCl_3$	4.06 (s)	 5.38 3.7 c.p.s.	7.66		8.68	−0.11	9.06	−0.03
6α-Acetylthioandrost-4-ene-3,17-dione (VIa)	$CHCl_3$	3.92 (d) $J=1.7$ c.p.s.	 5.59 $J_{4,6}=1.7$ $J_{e,a}=4.6$ $J_{a,a}=12.9$ c.p.s.	7.64		8.67	−0.12	9.07	−0.02
Testosterone acetate	$CDCl_3$	4.28 (s)	 5.39 $J=7.8$ c.p.s.		7.96	8.80		9.16	
6β-Acetylthiotestosterone acetate (Vb)	$CDCl_3$	4.07 (s)	 5.39 $J=7.8$ c.p.s.	7.67	7.95	8.69	−0.11	9.13	−0.03
6α-Acetylthiotestosterone acetate (VIb)	$CDCl_3$	3.92 (d) $J=1.7$ c.p.s.	 5.41 5.76 $J_{4,6}=1.7$ $J_{e,a}=4.6$ c.p.s.	7.65	7.95	8.69	−0.11	9.14	−0.02

s : singlet d : doublet

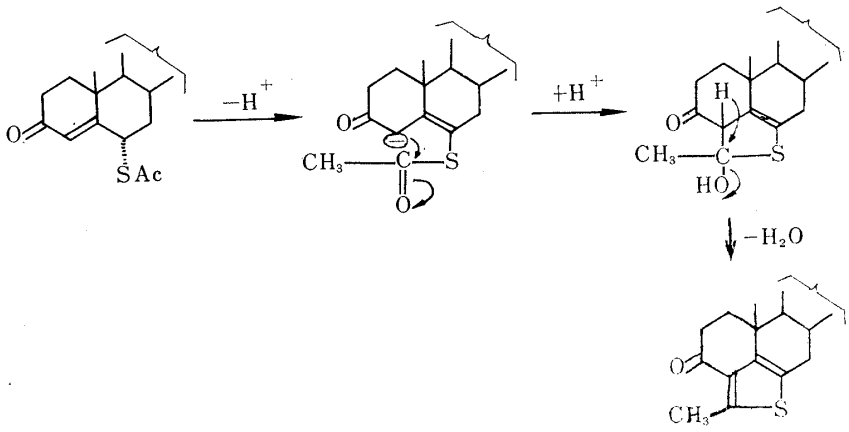


Chart 3.

*4 It was reported that 6β-acetoxy-4-en-3-one causes a 4 c.p.s. downward shift for the 19-methyl signal compared with 6α-epimer. Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, K. Tsuda : This Bulletin, **10**, 338 (1962).

The shift of the proton signal of the C_{19}-methyl is not observed in Vb and Vc, when compared with that of VIb and VIc.*4 In the case of IVa or IVc, when the 6β-acetylthio-5α-ol derivative was treated with hydrochloric acid in acetic acid, it gave the epimerized enone (VIa or VIc) directly, where dehydration and epimerization occurred in one step.

The intramolecular condensation reaction of such 6α-acetylthio steroids may proceed by the following mechanism. This reaction does not proceed with triethylamine but with sodium ethoxide in absolute ethanol. VIIa and VIIb showed no remarkable hormonal activity.

Experimental*5

Cholestenone Series

5α-Hydroxy-6β-acetylthiocholestan-3-one (IV)——A solution of 6.30 g. of α-oxide (III)[14] in 20 cc. of AcSH was allowed to stand for 61 hr. at room temperature. The reaction mixture was evaporated to dryness *in vacuo* and the residue, dissolved in a mixture of 55 cc. of AcOH and 10 cc. of H_2O, was heated on a steam bath for 30 min. and gave precipitates. To the mixture H_2O was added and extracted with Et_2O. The ethereal solution was washed with 5% NaOH and H_2O, dried over Na_2SO_4, and evaporated to dryness. The residue was recrystallized from MeOH to give 6.18 g. of IV as needles, m.p. 184~186°. An analytical sample was further recrystallized from MeOH to give needles, m.p. 185~186°. $[\alpha]_D^{30}$ −56.4±3°(c=0.844, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{48}O_3S$: C, 73.06; H, 10.15; S, 6.73. Found: C, 73.26; H, 10.14; S, 6.75. UV λ_{max}^{EtOH} mμ (ε): 234 (4,720), 305 (230). IR ν_{max}^{Nujol} cm^{-1}: 3421 (OH), 1707, 1702, 1136, 1119 (3C=O & S-Ac),

6β-Acetylthiocholest-4-en-3-one (V)——To a solution of 1.443 g. of IV in 14 cc. of pyridine, 0.70 cc. of $SOCl_2$ was added dropwise with stirring at 0°. After agitation for 10 min., the reaction mixture was poured into ice and H_2O, and extracted with Et_2O-benzene. The organic solution was washed with 5% HCl, H_2O, 5% Na_2CO_3 solution, and then H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue dissolved in Et_2O was decolorized by Norit. and crystallized from pentane to give 979 mg. of V as needles, m.p. 102~105°. An analytical sample was prepared by recrystallization from MeOH to give needles, m.p. 106~107°. $[\alpha]_D^{29}$ +168.5°±3 (c=0.874, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{46}O_2S$: C, 75.93; H, 10.11; S, 6.99. Found: C, 76.13; H, 10.20; S, 6.93. UV λ_{max}^{EtOH} 240 mμ (ε 15,320). IR ν_{max}^{Nujol} cm^{-1}: 1693, 1124 (S-Ac), 1672, 1612 (4-en-3-one).

5′-Methylthieno[4′,3′,2′-4,5,6]cholest-5-en-3-one (VII)——A solution of 2.98 g. of V and 310 mg. of *p*-toluenesulfonic acid monohydrate in 30 cc. of AcOH was allowed to stand for 2 days at room temperature. To the reaction mixture H_2O was added and extracted with Et_2O. The ethereal solution was washed with H_2O, 5% Na_2CO_3 solution, and H_2O, dried over Na_2SO_4, evaporated to dryness, and gave 3.01 g. of oily residue, which exhibited an absorption maximum at 235 mμ in UV. The residue was dissolved in petr. ether and was chromatographed over 90 g. of Al_2O_3. The eluate (1.516 g.) with petr. ether-benzene (4:1) was recrystallized from Et_2O-MeOH to give 1.448 g. of VII as prisms, m.p. 131~132°. $[\alpha]_D^{29}$ −11±3°(c=0.866, $CHCl_3$). *Anal.* Calcd, for $C_{29}H_{44}OS$: C, 79.04; H, 10.07; S, 7.28. Found: C, 78.91; H, 10.03; S, 7.40. UV λ_{max}^{Nujol} mμ (ε): 221 (12630), 269 (11470), 305 (2280). IR ν_{max}^{Nujol} cm^{-1}: 1671, 1572, 1497. $\nu_{max}^{CHCl_3}$ cm^{-1}: 1658, 1574, 1493.

The semicarbazone of this compound was obtained by the usual method and was recrystallized from CH_2Cl_2-MeOH as fine needles, m.p. 283~285°(decomp.). *Anal.* Calcd. for $C_{30}H_{47}ON_3S$: C, 72.38; H, 9.52; N, 8.44. ; S, 6.44. Found: C, 72.52; H, 9.65; N, 8.51; S, 6.47. UV λ_{max}^{EtOH} mμ (ε): 230 (sh.) (18640), 236.5 (21070), 243.5 (sh.) (18110), 287 (16870).

Progesterone Series

5α-Hydroxy-6β-acetylthioallopregnane-3,20-dione (IVa)——5α,6α-Oxide (IIIa)[14] (6.2 g.) was dissolved in 32 cc. of AcSH and the reaction mixture was allowed to stand for 114 hr. at room temperature. The mixture was evaporated to dryness *in vacuo*, dissolved into a mixture of 50 cc. of AcOH and 20 cc. of H_2O, and was heated on a steam bath for 2 hr. When the solution was concentrated under reduced pressure, crystals appeared and then H_2O was added. The precipitates were collected by filtration, dried, and heated with 20 cc. of Ac_2O and 10 cc. of pyridine for 1 hr. To the mixture H_2O

*5 All melting points are uncorrected. Infrared spectra were measured with a Koken Infrared Spectrophotometer, Model DS-301, and Ultraviolet spectra were taken with a Hitachi Recording Ultraviolet Spectrophotometer, EPS-2. Optical rotations were measured with a Rudolf Photoelectronic Polarimeter, Medel 200, and R.D. curves were taken with a Rudolf automatic recording spectropolarimeter.

14) G. Cooley, B. Ellis, D.N. Kirk, V. Petrow: J. Chem. Soc., **1957**, 4112.

and ice were added and the precipitates were collected by filtration and recrystallized from Me_2CO to give 4.0 g. of IVa as prisms, m.p. 227~229°. $[\alpha]_D^{27}$ −27±2°(c=1.130, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{34}O_4S$: C, 67.94; H, 8.43; S, 7.89. Found: C, 67.89; H, 8.30; S, 7.84. UV: λ_{max}^{EtOH} 234 mμ (ε 5890). IR ν_{max}^{Nujol} cm^{-1}: 3234 (OH), 1706 (sh.), 1691 (C=O), 1677, 1122 (S-Ac). $\nu_{max}^{CS_2}$ cm^{-1}: 1700 (sh.), 1695, 1123.

The mother liquor (1.70 g.) was chromatographed over 50 g. of Florisil and the eluate with petr. ether-benzene (1:1) and benzene was crystallized from MeOH to give 560 mg. of needles, m.p. 175~180°, which were identified to be the same as Va in the following experiment by mixed melting point and comparison of the IR spectrum. The eluate with benzene-Et_2O and Et_2O-$CHCl_3$ was crystallized from Me_2CO to give 370 mg. of IVa as prisms, m.p. 227~229°. Total yield of IVa: 4.37 g.

6β-Acetylthioprogesterone (Va)——To a solution of 2.00 g. of IVa in 20 cc. of pyridine, 1.0 cc. of $SOCl_2$ was added dropwise with stirring at 0°. After agitation for 5 min., ice and dil. HCl was added to the reaction mixture and extracted with $CHCl_3$. The $CHCl_3$ solution was washed to neutrality, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue was recrystallized from MeOH to give 1.25 g. of Va as silky needles, m.p. 185~187°. $[\alpha]_D^{25}$ +243±2°(c=1.06, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{32}O_3S$: C 71.09; H, 8.30; S, 8.25. Found: C, 71.54; H, 8.46; S, 8.07. UV: λ_{max}^{EtOH} 238 mμ (ε 15140). IR ν_{max}^{Nujol} cm^{-1}: 1695, 1118 (20 C=O & S-Ac), 1660, 1611 (4-en-3-one). $\nu_{max}^{CHCl_3}$ cm^{-1}: 1698 (sh.), 1690, 1676 (sh.), 1610, 1123.

In another run, 320 mg. of IVa was treated with 0.35 cc. of $SOCl_2$ in 10 cc. of pyridine and 170 mg. of Va was obtained. Chromatography over Al_2O_3 of the mother liquor gave the compound, m.p. 163~164°, which was identified as VIIa obtained in the following experiment by mixed melting point and comparison of the IR spectrum.

5'-Methylthieno[4',3',2'-4,5,6-]pregn-5-ene-3,20-dione (VIIa)——a) From the α-hydroxy-acetylthio compound (IVa): To a solution of 300 mg. of IVa in 15 cc. of AcOH, dry-HCl was bubbled for 1 hr. The mixture was allowed to stand overnight at room temperature, H_2O was added, and extracted with Et_2O. The ethereal solution was washed with 5% Na_2CO_3 solution and H_2O, dried over anhyd. Na_2SO_4, and evaporated. The residue, which exhibited an absorption maximum at 236 mμ in UV, was chromatographed over 7 g. of Al_2O_3. The eluate with benzene was crystallized from MeOH to give 100 mg. of VIIa as prisms, m.p. 163~164°. $[\alpha]_D^{30}$ +38.1±3°(c=0.862, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{30}O_2S$: C, 74.55; H, 8.16; S, 8.65. Found: C, 74.81; H, 8.11; S, 8.99. UV λ_{max}^{EtOH} mμ (ε): 221 (13480), 268 (12370), 302 (2670), $\lambda_{max}^{CHCl_3}$ mμ: 270, 304, $\lambda_{max}^{dioxane}$ mμ (ε): 267 (11420), 298 (2590). IR ν_{max}^{Nujol} cm^{-1}: 1702 (20 C=O), 1669, 1576, 1499. $\nu_{max}^{CHCl_3}$ cm^{-1}: 1696, 1663, 1570, 1491. M.W. by Rast: 379.5 (theoretical M.W.: 370.579).

b) From 6β-acetylthioprogesterone (Va): A solution of 500 mg. of Va and 100 mg. of *p*-toluenesulfonic acid monohydrate in 10 cc. of AcOH was allowed to stand overnight at room temperature and extracted with Et_2O. The oily product, which exhibited an absorption maximum at 235 mμ in UV, was crystallized from MeOH to give 170 mg. of recovered Va, m.p. 163~175°. The mother liquor (318 mg.) was chromatographed over Al_2O_3 and the eluate with benzene was recrystallized from MeOH to give 190 mg. of VIIa as prisms, m.p. 163~164°. This compound was identified as the above described compound by mixed melting point and comparison of the IR spectrum.

Testosterone Series

5α-17β-Dihydroxy-6β-acetylthioandrostan-3-one 17-Acetate (IVb)——A solution of 7.557 g. of α-oxide (IIIb)[15] in 30 cc. of AcSH was allowed to stand for 3 days at room temperature. The reaction mixture was evaporated to dryness *in vacuo* and the residue, dissolved in a mixture of 80 cc. of AcOH and 15 cc. of H_2O, was heated on a steam bath for 1 hr. To the mixture H_2O was added and extracted with Et_2O. The ethereal solution was washed with 5% NaOH and H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue was reacetylated with 10 cc. of Ac_2O and 30 cc. of pyridine. The product was crystallized from Et_2O-petr. ether to give 6.103 g. of IVb as needles, m.p. 223~225°. The mother liquor (1.891 g.) was chromatographed over 40 g. of Florisil and the eluates with benzene and Et_2O gave further 428 mg. of IVb as needles, m.p. 223~225°. An analytical sample was recrystallized from Me_2CO-hexane to give needles, m.p. 225~226°. $[\alpha]_D^{24}$ −83.1±2°(c=1.030, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{34}O_5S$: C, 65.37; H, 8.11; S, 7.59. Found: C, 65.37; H, 8.18; S, 7.61. UV λ_{max}^{EtOH} 233.5 mμ (ε 5140). IR ν_{max}^{Nujol} cm^{-1}: 3454 (OH), 1724, 1277, 1252 (3 C=O & OAc), 1688, 1136, 1120 (S-Ac).

6β-Acetylthiotestosterone Acetate (Vb)——To a solution of 6.531 g. of IVb in 65 cc. of pyridine, 4 cc. of $SOCl_2$ was added dropwise with stirring at 0°. After agitation for 15 min., ice and H_2O was added to the mixture and extracted with Et_2O. The ethereal solution was washed with 5% HCl, H_2O, 5% Na_2CO_3, and H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue (4.75 g.) was crystallized from Me_2CO-hexane to give 2.55 g. of Vb as small needles, m.p. 142~145°. The mother liquor (2.20 g.) was chromatographed over 40 g. of Florisil and gave further 205 mg. of crystals Vb, m.p, 143~145°, from the eluate with benzene-petr. ether (1:1). An analytical sample was prepared by recrystallization

15) A. Bowers, L.C. Ibanez, H.J. Ringold: Tetrahedron, **7**, 138 (1959).

from Me_2CO-hexane, m.p. 144~145°. $[\alpha]_D^{24}$ +186.5±2°(c=1.026, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{32}O_4S$: C, 68.28; H, 7.97; S, 7.93. Found: C, 68.54; H, 8.04; S, 7.82. UV λ_{max}^{EtOH} 237 mμ (ε 15960). IR ν_{max}^{Nujol} cm^{-1}: 1731, 1255, 1049, 1038 (OAc), 1691, 1124 (S-Ac), 1679, 1608 (4-en-3-one). $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1698, 1683, 1614, 1243, 1132, 1046, 1040. Rotatory dispersion curve (c=0.248 in dioxane): $[\alpha]_{700}$ +121°, $[\alpha]_{384}$ +1161°, $[\alpha]_{377}$ +1040°, $[\alpha]_{367}$ +1129°, $[\alpha]_{355}$ +831°, $[\alpha]_{340}$ +532°, $[\alpha]_{336}$ +589°, $[\alpha]_{329}$ +528°, $[\alpha]_{280}$ +3044°, $[\alpha]_{275}$ +1613°.

6α-Acetylthiotestosterone Acetate (VIb)——A solution of 2.755 g. of Vb and 600 mg. of *p*-toluenesulfonic acid monohydrate in 30 cc. of AcOH was allowed to stand for 2 days at room temperature. To the reaction mixture H_2O was added and extracted with Et_2O. The neutral extract was chromatographed over 60 g. of Florisil. The eluates with benzene and benzene-Et_2O (9:1~4:1) gave 1.972 g. of crystals from Et_2O-petr. ether, m.p. 182~185°. Recrystallization of this compound from MeOH gave 1.241 g. of IVc, m.p. 184~186°. An analytical sample was recrystallized from Me_2CO-hexane to give prisms, m.p. 192~194°. $[\alpha]_D^{22.5}$ +40.3±2°(c=1.016, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{32}O_4S$: C, 68.28; H, 7.97; S, 7.93. Found: C, 68.39; H, 8.10; S, 7.89. UV: λ_{max}^{EtOH} 235 mμ (ε 16820). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1741, 1244, 1044, 1016 (OAc), 1687, 1618, 1134 (S-Ac & 4-en-3-one). Rotatory dispersion curve (c=0.240 in dioxane): $[\alpha]_{700}$ +16.7°, $[\alpha]_{370}$ −333°, $[\alpha]_{363}$ −313°, $[\alpha]_{355}$ −429°, $[\alpha]_{345}$ −25°, $[\alpha]_{305}$ +1133°, $[\alpha]_{280}$ +125°.

17β-Hydroxy-5′-methylthieno[4′,3′,2′-4,5,6]androst-5-en-3-one Acetate (VIIb)——The pure compound (VIb) (1.001 g.) was adsorbed in benzene-petr. ether (1:3) over 30 g. of Al_2O_3. The eluates with petr. ether-benzene (1:1) and benzene gave 599 mg. of VIIb, m.p. 146~147°, from MeOH. An analytical sample was recrystallized from Me_2CO-hexane to give rods, m.p. 147~148°. $[\alpha]_D^{24.5}$ −33.0±2°(c=1.047, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{30}O_3S$: C, 71.46; H, 7.82; S, 8.30. Found: C, 71.26; H, 7.97; S, 8.59. UV λ_{max}^{EtOH} mμ (ε): 221 (12900), 268.5 (12740), 304 (2440). IR ν_{max}^{Nujol} cm^{-1}: 1732, 1268, 1252, 1049, 1034 (OAc), 1672, 1574, 1491. $\nu_{max}^{CHCl_3}$ cm^{-1}: 1726, 1664, 1575, 1495, 1035.

When this substance (VIIb) was saponified by refluxing with 300 mg. of K_2CO_3 in 80% MeOH for 2 hr., 125 mg. of 17-ol, m.p. 208~210°, was obtained as prisms by recrystallization from Me_2CO-hexane. $[\alpha]_D^{24}$ −27.4°(c=1.067, EtOH). *Anal.* Calcd. for $C_{21}H_{28}O_2S$: C, 73.21; H, 8.19; S, 9.31. Found: C, 73.30; H, 8.15; S, 9.35. UV λ_{max}^{EtOH} mμ (ε): 221 (12550), 268.5 (11740), 304 (2360). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620, 3354, 1051 (OH), 1665, 1573, 1494.

Epoxidation of 3,3,17,17-Bisethylenedioxyandrost-5-ene——To a solution of 13.25 g. of 3,3,17,17-bisethylenedioxyandrost-5-ene, 110 cc. of $C_6H_4(CO_2H)CO_3H$-ether solution (0.44*M*) was added under cooling and the reaction mixture was allowed to stand for 6 days in a refrigerator. After treatment as usual the product was recrystallized from 100 cc. of Me_2CO to yield 5.0 g. of needles, which were further recrystallized twice from Me_2CO to 4.45 g. of pure α-oxide (IIIc), m.p. 212~214°, as needles. $[\alpha]_D^{21}$ −84.1±2°(c=1.027, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.68; H, 8.96. IR: ν_{max}^{Nujol} 1098 cm^{-1} (ketal).

The mother liquor was evaporated to dryness and chromatographed over 300 g. of Al_2O_3. The residue from the earlier eluate was recrystallized from MeOH and further from aq. EtOH to yield 4.60 g. of pure β-oxide, m.p. 137~138°, as flat needles, $[\alpha]_D^{21}$ −26.7±2°(c=1.068, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.61; H, 8.84. IR: ν_{max}^{Nujol} 1106 cm^{-1} (ketal).

5α-Hydroxy-6β-acetylthioandrostane-3,17-dione (IVc)——A solution of 4.036 g. of the α-oxide (IIIc) in 18 cc. of AcSH was allowed to stand for 87 hr. at room temperature. The reaction mixture was evaporated *in vacuo*, dissolved in 20 cc. of AcOH, and again evaporated *in vacuo*. The residue was dissolved in 50 cc. of 80% AcOH and warmed on a steam-bath for 30 min. H_2O was added and the appeared precipitates were collected by filtration. Recrystallization from Me_2CO-hexane gave 3.244 g. of IVc, m.p. 233~237°, as needles. Recrystallization from aq. MeOH gave an analytical sample as needles, m.p. 238~240°. $[\alpha]_D^{23}$ −14.0±2°(c=1.028, $CHCl_3$). *Anal.* Calcd. for $C_{21}H_{30}O_4S$: C, 66.63; H, 7.99; S, 8.47. Found: C, 66.43; H, 8.04; S, 8.62. UV λ_{max}^{EtOH} mμ (ε): 234 (5010), 308 (490). IR ν_{max}^{Nujol} cm^{-1}: 3366 (OH), 1739 (17-one), 1707, 1137, 1114 (3-one and S-Ac).

6β-Acetylthioandrost-4-ene-3,17-dione (Vc)——To a solution of 2.008 g. of IVc in 60 cc. of pyridine, 1.00 g. of $SOCl_2$ was added dropwise with stirring at −5°. After agitation for 10 min. at −2° the reaction mixture was poured into ice and H_2O, and extracted with Et_2O. The ethereal solution was washed with 5% HCl, H_2O, 5% Na_2CO_3, and H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue amounting to 1.863 g. was recrystallized from Me_2CO-hexane to yield 1.561 g. of Vc, m.p. 163~165°, as needles. Recrystallization from MeOH and further from Me_2CO-hexane gave an analytical samle, m.p. 170~171°, as needles. $[\alpha]_D^{23}$ +298.8±2°(c=1.005, $CHCl_3$). *Anal.* Calcd, for $C_{21}H_{28}O_3S$: C, 69.96; H, 7.83; S, 8.89. Found: C, 70.30; H, 7.97; S, 8.82. UV: λ_{max}^{EtOH} 237 mμ (ε 15820). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1737 (17-one), 1689 (sh.), 1117 (S-Ac), 1678, 1617 (4-en-3-one).

6α-Acetylthioandrost-4-ene-3,17-dione (VIc)——a) From 5α-hydroxy-6β-acetylthioandrostane-3,17-dione (IVc): Into a solution of 589 mg. of IVc in 20 cc. of AcOH, dry HCl was passed for 45 min. To the reaction mixture H_2O was added and extracted with Et_2O. The ethereal solution was washed with

5% Na_2CO_3 and H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue amounting to 551 mg. could not be crystallized from any solvents.

b) From 6β-acetylthioandrost-4-ene-3,17-dione (Vc): A solution of 1.283 g. of Vc and 205 mg. of *p*-toluenesulfonic acid monohydrate in 30 cc. of AcOH was allowed to stand for 2 days at room temperature. To the reaction mixture H_2O was added and extracted with Et_2O. The ethereal solution was washed with H_2O, 5% Na_2CO_3 and H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue was twice chromatographed over Florisil. The main product (927 mg.) was an oil, which could not be crystallized. Besides this oil, 268 mg. of Vc was recovered from the above chromatography. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1736, 1688 (sh.), 1679, 1616, 1125. UV: λ_{max}^{EtOH} 235 mμ (ε 15650).

5'-Methylthieno[4',3',2'-4,5,6]androst-5-ene-3,17-dione (VIId)——The oil (551 mg.) obtained in the above (a) was chromatographed over 10 g. of Al_2O_3. The eluate with petr. ether-benzene (1:1) and benzene was crystallized from Et_2O to give 192 mg. of crystals. Recrystallization from Me_2CO gave pure VIId, m.p. 234~235°, as needles. $[\alpha]_D^{23.5}$ + 38.9 ± 2° (c=1.027, $CHCl_3$). *Anal.* Calcd. for $C_{21}H_{26}O_2S$: C, 73.64; H, 7.65; S, 9.36. Found: C, 73.75; H, 7.68; S, 9.35. UV λ_{max}^{EtOH} mμ (ε): 221 (13730), 268.5 (12240), 304 (sh.) (2710). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1664, 1573, 1493.

The oil (769 mg.) obtained in the above (b) was chromatographed over Al_2O_3 also to yield 350 mg. of VIId, m.p. 234~235°.

Attempted Reaction of the Intramolecular Cyclization with Sodium Ethoxide or Triethylamine——a) By sodium ethoxide: The oily VIa obtained from 200 mg. of IVa by AcOH-HCl, was dissolved in 10 cc. of abs. EtOH, and 9 cc. of 15% EtONa-EtOH solution was added. The reaction mixture was allowed to stand at room temperature overnight. Formation of VIIa was checked by IR spectrum. The mixture was further warmed on a steam-bath for 1.5 hr., poured into H_2O, acidified by 10% HCl, and extracted with Et_2O. The ethereal solution was washed with H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue (140 mg.) was chromatographed over 6 g. of Florisil. From the eluate with benzen-Et_2O (9:1) 65 mg. of crude VIIa, m.p. 150~163°, was obtained. Recrystallization from MeOH gave 43.7 mg. of pure VIIa, m.p. 165~167°, which was characterized by mixed melting point and IR spectrum comparison.

b) By triethylamine: The oily VIa (300 mg.) was dissolved in 30 cc. of anhyd. NEt_3. Formation of VIIa was checked by IR spectrum under the following condition. In all cases the starting material was recovered. 1) Standing for 4 hr. at room temperature. 2) Standing overnight and warming on a steam bath for 1 hr. 3) Standing for 8 days at room temperature.

Experiments on the Structure of VII

5'-Methylthieno[4',3',2'-4,5,6]cholest-5-ene (VIII)——A solution of 100 mg. of VII, 1 cc. of 80% $NH_2NH_2 \cdot H_2O$, and 300 mg. of KOH in 10 cc. of triethyleneglycol was refluxed for 1 hr., distilled until the inner temperature reached 200°, and further heated at the same temperature for 3 hr. After cooling, H_2O was added to the reaction mixture and extracted with Et_2O. The extract (99 mg.)was chromatographed over 5 g. of Al_2O_3. The eluates with petr. ether yielded 83 mg. of crystals VIII, m.p. 95~96°, recrystallized from Me_2CO-MeOH. $[\alpha]_D^{24}$ +17.9±2°(c=1.011, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{46}S$: C, 81.62; H, 10.87; S, 7.51. Found: C, 81.63; H, 10.93; S, 7.48. UV λ_{max}^{EtOH} 246 mμ (ε 8870).

This compound has no characteristic absorption band in IR spectrum, but an absorption band at 1595~1600 cm^{-1} in the Raman spectrum.

Desulfurization of VII——A suspension of 302 mg. of VII and 3 g. (wet weight) of freshly prepared W-2 Raney-Ni in 5 cc. of dioxane was heated on a steam bath for 10 hr. After cooling, H_2O was added to the solution filtered off Ni and the precipitates were collected by filtration. The product was recrystallized from Me_2CO to give 149 mg. of IX as needles, m.p. 167~170°. An analytical sample was further recrystallized from $CHCl_3$-MeOH to give needles, m.p. 170~171°. $[\alpha]_D^{29}$ +6.4±2° (c=0.951, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{52}O$: C, 83.58; H, 12.58. Found: C, 83.78; H, 12.49. IR $\nu_{max}^{CS_2}$ cm^{-1}: 3628, 1039, 997 (ω).

When this compound was reduced with PtO_2 in AcOH, unchanged IX was recovered.

4α-Ethylcholestan-3-one (X)——To a solution of 120 mg. of IX in a mixture of 4 cc. of AcOH and 4 cc. of $CHCl_3$, 20 mg. of CrO_3 was added. The reaction mixture was allowed to stand overnight at room temperature. The neutral fraction (109 mg.) obtained by the usual method was chromatographed over 3 g. of Al_2O_3. The eluates with petr. ether-benzene (1:1) were recrystallized from MeOH to give leaflets, m.p, 120~122°. It was identified by mixed melting point and comparison of the IR spectrum with the authentic sample that the compound was 4α-ethylcholest-3-one. $[\alpha]_D^{21}$ +38.3±3° (c=0.716, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{50}O$: C, 83.99; H, 12.15. Found: C, 84.08; H, 12.10. IR: ν_{max}^{Nujol} 1712 cm^{-1}. Rotatory dispersion curve (c=0.1009 in MeOH), (c=0.1109 in HCl-MeOH) (see Fig. 3). Reported by Brown:[6] m.p. 120.5~121°, $[\alpha]_D$ +33°, IR $\nu_{max}^{CHCl_3}$ 1720 cm^{-1}; Reported by Djerassi:[5] m.p. 120~122°, $[\alpha]_D$ +38°, IR: ν_{max}^{CHCl3} 1720 cm^{-1}. Rotatory dispersion curve:[5] in dioxane: $[\alpha]_{700}$ +27°, $[\alpha]_{589}$ +44°, $[\alpha]_{317.5}$ +864°, $[\alpha]_{277.5}$ −633°, $[\alpha]_{275}$ −496°.

The authentic sample was prepared by the method described by Brown[6] and Djerassi[5] from cholestenone. Our obtained 4α-ethylcholestan-3-one showed the following physical constants. m.p. 120~121°, $[\alpha]_D^{21}$ +36.0±2°(c=0.918, $CHCl_3$).

4α-Ethylcholestane (XI)——The ketone (44 mg.) obtained from the desulfurization product of Ⅶ was treated with 0.2 g. of KOH, 0.4 cc. of $NH_2NH_2 \cdot H_2O$, and 4 cc. of triethyleneglycol in the same manner as for the preparation of Ⅷ. The product was purified by passing through a column of 1 g. of Al_2O_3 in a petr. ether solution, and was recrystallized from Et_2O-MeOH to give 30 mg. of needles, m.p. 86~88°. $[\alpha]_D^{24}$ +10.9±4°(c=0.594, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{52}$: C, 86.92; H, 13.08. Found: C, 87.19; H, 13.11.

This compound was identified as 4α-ethylcholestane by mixed melting point and comparison of the IR spectrum with that of the authentic sample. The authentic sample was prepared by the Huang-Minlon reduction of 4α-ethylcholestan-3-one prepared from cholestenone and showed the following physical constants. m.p. 86~88°. $[\alpha]_D^{24}$ +12.3±2°(c=1.058, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{52}$: C, 86.92; H, 13.08. Found: C, 86.64; H, 12.94. Reported by Brown, m.p. 89~90°, $[\alpha]_D$ +4.5°, +6°.

Summary

The 3,3-ethylenedioxy-5α,6α-epoxy steroids were converted to the 5α-hydroxy-6β-acetylthio-3-oxo steroids by the action of thiolacetic acid. These were dehydrated, and following by epimerization of the substituent at position 6 converted to 6α-acetylthio-4-en-3-one steroids. The thiophene derivatives were obtained from the last mentioned compounds by the action of basic alumina.

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91. Kiyoshi Tsuneda, Joji Yamada, Kikuo Yasuda, and Hiromu Mori: Preparation of Some Estriol Esters.

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In some cases esters of steroidal hormones show long-acting hormonal activities compared with the parent hormones. In the hope of preparing long-acting steroidal hormones, many esters of steroidal hormones such as testosterone, estradiol and others, have been prepared and then activities have been studied.[1] Nevertheless, no estriol ester, except the triacetate[2] and 3,16-diacetate[3] has beenpre pared. It is interesting to prepare various estriol esters and study about their activities. In the present paper, the preparation of some esters of estriol will be described.

In 1956 it was reported from this laboratory that estradiol is acylated only at C-17-hydroxyl group by reflux with a carboxylic acid[4] or by transesterification[5] to give estradiol 17-monoacylate. When estriol (I) was treated with acetic acid or with methyl acetate (transesterification), in the same way, a material (Ⅱa), m.p. 190~193°, was obtained. Elemental analysis showed it is an estriol monoacetate. In order to deter-

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