is present. In addition, the vinyl proton region (near $\tau = 4$) shows both the pair of doublets associated with the exocyclic methylene group of the lactone and additional vinyl peaks for $=\text{CH}-$, probably affected by the adjacent $-\text{CH}_2$-grouping and perhaps by the side chain, in the same region of the spectrum. Were structure III the correct one, there would be no additional vinyl hydrogen signals besides those of the $=\text{CH}_2$ group.

The explanation for the results of the degradation experiments described by the Šorm group is obscure, but there can be no doubt that xanthinin has indeed the structure I, despite the Czech findings.

Configurations of 1- and 7-Acetylthio-4-androstene-3,17-diones

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In a previous paper[1] the preparation of a number of 1α- and 7α-acetylthio-Δ^4-3-oxo steroids was reported. At that time the configurations at 1 and 7 were assigned on the basis of analogy in the absence of more definitive evidence. Since NMR spectra have now been used to assign configurations in a similar series of steroidal esters,[2] we decided to examine the curves of some of the sulfur compounds. The substituted 4-androstene-3,17-diones were chosen as readily available models whose NMR spectra should not be too complicated.

In the previous paper,[1] the 7α-acetylthio compound was described as a glass. This result was apparently due to the presence in the starting 4,6-dien-3-one of an appreciable amount of 1,4-diene-3-one. The use of pure material gave, by chromatography and fractional crystallization, both the 7α- and 7β- isomers as crystalline solids. The molecular rotatory changes for the two compounds are consistent with the values reported for the corresponding oxygen esters.[2]

A definitive proof of the structures is proved by the NMR spectra.[3] The spectra of the thioesters (see Table I) are qualitatively quite similar to those of their oxygen analogs, whose structures have been discussed.[2] The peaks for the 7α- and 7β-acetoxymethyls and the 7β-hydrogen are quite close to Jackman's values for alicyclic acetates.[4] The acetylthio-methyls show a shift of about 0.25–0.30 p.p.m. to lower τ values, while the peaks of the protons on the same carbon atom as the sulfur atom are shifted 1.0–1.2 p.p.m. higher than the corresponding peaks in the oxygen analogs.

TABLE I

NMR SPECTRA OF ACETYLTHIO-4-ANDROSTENE-3,17-DIONES

	Position of Acetylthio Group			
	7α	7β	1α	1β
C_4-H	4.30	4.23	4.25	4.17
19-Methyl	8.75	8.79	8.60	8.70
18-Methyl	9.08	9.10	9.10	9.13
1- or 7-Thioacetyl methyl	7.65	7.68	7.68	7.67
1- or 7-Hydrogen	5.92	6.43 6.54	5.92	5.74

Since the β-isomer had been found at the 7-position, we decided to check the addition product from the 1,4-diene as well. A careful reëxamination of the preparation of 1α-acetylthio-4-androstene-3,17-dione also revealed the presence of the β- isomer in 9% yield. In the case of the 1-isomers, the NMR spectra did not provide conclusive evidence for the assigned configurations. The 1β-hydrogen gives a good singlet, but the 1α-hydrogen produces a peak intermediate in shape between a singlet and a multiplet, and the positions of the two peaks are reversed compared to those of the 7-isomers.

We then turned to rotations to provide more conclusive evidence. The molecular rotatory contribution of the 1β-acetylthio group is strongly negative as is the value for 1β-acetoxy 4-androstene-3,17-dione −358°,[5] while the contributions of the 1α-acetoxy and acetylthio groupings are positive.[1]

The rotatory dispersion curves[6] also confirm the configurational assignments. The curves for the 1α-compounds are very similar to each other and to 4-androstene-3,17-dione[7] (see Table II), but the amplitudes of the peaks of the 1β-isomers are considerably lower than those of the 1α-isomers.

The relative yield of the isomers may vary depending on the conditions of the reaction. In the addition of ethanethiolic acid to 17a-oxa-D-homo-1,4-androstadiene-3,17-dione, a total of 97% of the 1α-isomer was obtained. This high yield may be due to the long heating period or to the fact that the product had crystallized from the hot mixture.

Another compound, previously reported as a glass,[1] has now been obtained in crystalline form. This is 1α-acetylthiotestosterone, whose constants are given in the experimental section.

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[1] R. M. Dodson and R. C. Tweit, *J. Am. Chem. Soc.*, **81**, 1224 (1959).

[2] R. C. Tweit, A. H. Goldkamp, and R. M. Dodson, *J. Org. Chem.*, **26**, 2856 (1961).

[3] Very kindly determined and interpreted by Dr. N. L. McNiven of the Worcester Foundation for Experimental Biology. They were run at 60 mc. in deuterochloroform. The shifts are reported as τ values relative to tetramethylsilane as an internal standard [see G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958)].

[4] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, 1959, pp. 55–7.

[5] R. M. Dodson, S. Kraychy, R. T. Nicholson, and S. Mizuba, *J. Org. Chem.*, in press.

[6] Very kindly determined by Professor W. Klyne of Westfield College (University of London) and Professor C. Djerassi of Stanford University.

[7] C. Djerassi, E. W. Foltz, and A. E. Lippman, *J. Am. Chem. Soc.*, **77**, 4354 (1955).

TABLE II

OPTICAL ROTATORY DISPERSION CURVES OF 1-SUBSTITUTED ANDROSTENEDIONES

No substituent $\lambda[\phi]$	1α - OAc $\lambda[\phi]$	1α - SAc $\lambda[\phi]$	1β - OAc $\lambda[\phi]$	1β - SAc $\lambda[\phi]$
385 (1560)	400 (1240)	381 (1530)	...	...
367.5 (1170)	369 (480)	359 (1250)	...	...
320 (10,450)	317 (13,300)	310 (14,000)	315 (5750)	317.5 (3580)
Dioxane	Dioxane	Methanol	Methanol	Methanol

Experimental[8]

7α- and 7β-Acetylthio-4-androstene-3,17-dione.—4,6-Androstadiene-3,17-dione, 3.2 g., was mixed with 4 ml. of ethanethiolic acid and warmed on the steam bath for 0.5 hr. Then part of the excess acid was removed under vacuum and the residue was dissolved in benzene and chromatographed on 400 g. of silica gel. From the early fractions eluted with 10% ethyl acetate-benzene there was obtained 0.9 g. of 7α-acetylthio-4-androstene-3,17-dione by crystallization from ether, m.p. 158.5–160.5°, $[\alpha]_D$ +31 ± 1°, ΔM_D −455°, $\lambda_{max}^{CH_3OH}$ 237.5 mμ, ϵ 19,500.

Anal. Calcd. for $C_{21}H_{28}O_2S$: C, 69.96; H, 7.83. Found: C, 69.94; H, 7.83.

From another run a yield of 43% was obtained by direct crystallization.

From the later 10% fractions two types of crystals formed, prisms (the 7α-isomer) and needles. The needles were separated by hand and recrystallized several times from ether to yield 0.20 g. of 7β-acetylthio-4-androstene-3,17-dione, m.p. 129–132° dec., $[\alpha]_D$ +166°, ΔM_D +31°, $\lambda_{max}^{CH_3OH}$ 237 mμ, ϵ 17,400.

Anal. Found: C, 70,35; H, 7.86.

The remaining material was apparently a mixture of the two isomers, but further recovery of pure material was not attempted.

1α- and 1β-Acetylthio-4-androstene-3,17-dione.—1,4-Androstadiene-3,17-dione, 10.0 g., was mixed with 10 ml. of ethanethiolic acid and heated on the steam bath for 15 min. During this time, the solid dissolved and a new solid formed. Fractional crystallization of the material from methylene chloride–ether gave 10.6 g. (83%) of 1α-acetylthio-4-androstene-3,17-dione, same m.p. and infrared spectrum as previously reported material,[1] and 1.15 g. (9%) of 1β-acetylthio-4-androstene-3,17-dione, m.p. 177.5–179° dec., $[\alpha]_D$ 1 ± 1°, ΔM_D −564°, $\lambda_{max}^{CH_3OH}$ 240.5 mμ, ϵ 14,900.

Anal. Found: C, 69.76; H, 7.94.

1α-Acetylthiotestosterone.—17β-Hydroxy-1,4-androstadien-3-one, 2.2 g., was heated with 2 ml. of ethanethiolic acid for 20 min. on the steam bath. Ether was added and after 2 days crystals formed. They were recrystallized three times from acetone–ether–petroleum ether to yield 1.65 g. of 1α-acetylthiotestosterone, m.p. 138.5–139° dec., $\lambda_{max}^{CH_3OH}$ 241 mμ, ϵ 15,400, $[\alpha]_D$ +128.5°, ΔM_D +126°.

Anal. Calcd. for $C_{21}H_{30}O_2S$: C, 69.57; H, 8.34. Found: C, 69.90; H, 8.40.

Another 0.25 g. of material, m.p. 136.5–138° dec. was obtained from the mother liquors. Chromatography of the residue gave 0.15 g. of impure solid as well as noncrystalline material which may have included the β isomer.

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[8] Rotations taken in chloroform at 24 ± 2°.

Synthesis of (+)-9-Methyl-*trans*-1,4,9,10-tetrahydronaphthalene

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As part of a research program on the optical rotatory dispersion of nonplanar conjugated dienes,[1] a substance was required on which theoretical predictions of the sign and intensity of the Cotton effect could be tested. The substance had to satisfy the following requirements: Its absolute configuration had to be known, and it had to contain a nonplanar, conformationally fixed cisoid dienic system; furthermore, its structure had to be sufficiently simple for theoretical calculations to be manageable, and the compound had to be available in high optical purity.

These conditions are satisfied by (+)-9-methyl-*trans*-1,4,9,10-tetrahydronaphthalene (I). Dreiding models show that the conformationally rigid diene system of I deviates from planarity by an angle of about 17.5°, the skewness[2] corresponding to that of a right-handed helix. The structural element II present in compound I is quite unusual; we are aware of only one other compound embodying this feature, *viz.*, the 1,3-cholestadiene of Tamm and Albrecht.[3] In particular, the $\Delta^{1,3}$-arrangement does not seem to be represented among the numerous natural sesqui-, di-, and triterpenes. This fact suggested that structure II might be markedly unstable, and that compounds containing it might be quite difficult to prepare. The desired substance

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[1] A. Moscowitz, E. Charney, U. Weiss, and H. Ziffer, *J. Am. Chem. Soc.*, **83**, 4661 (1961).

[2] Theory (1) predicts that the skewness (*i.e.*, sense of helicity) governs the sign of the Cotton effect, as its contribution to the rotation far outweighs that of asymmetric substituents; a right-handed helicity produces a positive Cotton effect.

[3] Ch. Tamm and R. Albrecht, *Helv. Chim. Acta*, **42**, 2177 (1959).