and the separated solid was collected by filtration, washed repeatedly (H_2O), and dried. On crystallizing from boiling H_2O, 3.2 g of an orange-colored product, mp 174–175° was obtained. *Anal.* ($C_{15}H_{16}O_5$) C, H.

3,6-Dihydroxy-4,5-dimethylxanthone.—Following the procedure of Grover, *et al.*,[22] 2.5 g of 2,2',4,4'-tetrahydroxy-3,3'-dimethylbenzophenone in 25 ml of H_2O, was heated in an autoclave at 200–220° for 2.5 hr. After cooling the 3,6-dihydroxy-4,5-dimethylxanthone was collected and dried. It did not melt below 310°. *Anal.* ($C_{15}H_{14}O_4$) C, H.

3-Propionoxyxanthone.—A mixture of 4 g of 3-hydroxyxanthone[24] and 10 ml of Pr_2O was refluxed for 1 hr and then poured into ice-H_2O. The separated solid was collected by filtration, washed (H_2O), and dried. On crystallizing from ligroin, 3.1 g of white solid, mp 151–152°, was obtained. *Anal.* ($C_{16}H_{12}O_4$) C, H.

3-Hydroxy-4-propionylxanthone.—To a melt consisting of 1 g of NaCl and 3 g of $AlCl_3$, 1 g of 3-propionoxyxanthone was added and the temperature was kept at 160–170° for 4.5 min. The mixture was hydrolyzed with dil HCl and ice-H_2O, and the separated solid was collected and washed with H_2O. This was dissolved in dil NaOH and reprecipitated with dil HCl. The separated solid, on crystallizing from EtOH, gave 0.8 g of white product, mp 170–172°. *Anal.* ($C_{16}H_{12}O_4$) C, H.

(24) F. Ullmann and W. Denzler, *Chem. Ber.*, **39**, 4335 (1906).

2,3-Dimethyl-1H,7H-pyrano[2,3-*c*]xanthene-1,7-dione (III).—A mixture of 0.6 g of 3-hydroxy-4-propionylxanthone, 0.7 g of anhyd NaOAc, and 3 g of Ac_2O was refluxed for 8 hr. By pouring the reaction mixture into H_2O a solid was isolated, which on crystallizing from EtOH, gave 0.5 g of white product, mp 266–267°. *Anal.* ($C_{18}H_{12}O_4$) C, H.

3-Hydroxyxanthonyl-(4)-styril Ketone.—To a solution of 0.5 g of 3-hydroxy-4-acetylxanthone[25] and 0.2 ml of BzH in 30 ml of 95% EtOH, 5 ml of 50% aqueous KOH was added with stirring, and the mixture was left to stand 12 hr. After dilution with H_2O and acidification, the separated solid was collected, dried, and crystallized from ligroin yielding 0.5 g of light yellow product, mp 172–175°. *Anal.* ($C_{22}H_{14}O_4$) C, H.

3-Phenyl-1H,7H-pyrano-[2,3-*c*]xanthene-1,7-dione (IV).—A mixture of 0.2 g of the preceding product, 0.3 g of SeO_2, and 7 ml of AmOH was heated at 145° for 7 hr. After cooling, the reaction mixture was filtered and the collected solid (a mixture of Se and product) was extracted with EtOH to give 0.15 g of white solid, mp 272–273°. *Anal.* ($C_{22}H_{12}O_4$) C, H.

Acknowledgment.—The authors are indebted to Mr. G. Cilia for his technical assistance.

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Thia Steroids. III. Derivatives of 2-Thia-A-nor-5α-androstan-17β-ol As Probes of Steroid–Receptor Interactions[1]

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The preparation of analogs of 2-thia-A-nor-5α-androstan-17β-ol having three typical modifications used in anabolic–androgenic compounds, *viz.*, the introduction of a 7α-Me group, the 19-nor modification, and the introduction of a 17α-alkyl group, is described. In addition, the SO and SO_2 derivatives of the parent compound were prepared. Biological evaluation shows that the SO and SO_2 derivatives are inactive, and that the pharmacological effects of the other modifications on thiasteroids parallels their effects in the testosterone series. From this it is concluded that the three modifications affect drug–receptor interactions, and not drug distribution or drug metabolism. The effects of these groups may be direct, by interaction with the receptor, or indirect, by altering the conformation of the steroid itself through conformational transmission.

In a previous paper[2] of this series, the synthesis of 2-thia-A-nor-5α-androstan-17β-ol as an isostere of 17β-hydroxy-5α-androst-2-ene was described. The androgenic–anabolic activity of this compound was taken as evidence that *steric* effects, and not *electronic* factors, are important in connection with structural requirements at C-2 and/or C-3 in androgens. As described in the Discussion, the discovery of this new, biologically active ring system provides a powerful general tool in the examination of the relationship between chemical structure and biological activity in androgenic–anabolic steroids. For this reason, the preparation of thiasteroids having three typical enhancing groups used in anabolic–androgenic compounds, *viz.*, the 7α-Me group, the 19-nor modification, and the 17α-alkyl group, was undertaken. In addition, the sulfoxide and sulfone derivatives of 2-thia-A-nor-5α-androstan-17β-ol acetate were synthesized.

7α-Methyltestosterone[3] was prepared in 40% yield by an improved procedure and the reduction of the double bond in this compound was studied. Hydrogenation in the presence of PtO_2 gave a product which had a negative CD curve and a negative Cotton effect in the ORD. It was assigned the 5β configuration **2** on this basis.[4] The formation of **2** under these conditions is consistent[5] with interference by the axial 7α-Me group to adsorption of the α face of the steroid on the catalyst surface. By contrast, reduction of 7α-methyltestosterone with Li in liquid NH_3 cleanly gave the 5α-dihydro compound **3**, as shown by the positive CD and Cotton effect curves of the corresponding acetate **4**. The formation of **3** under conditions giving the thermodynamically favored isomer is in accord with the repulsive interaction in **2** of the 7α-Me group and the 1α-H, which is absent in **3**.

(1) This investigation was supported in part by a Public Health Service Research Grant (AM-05016) from the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service.

(2) M. E. Wolff and G. Zanati, *J. Med. Chem.*, **12**, 629 (1969).

(3) J. A. Campbell and J. C. Babcock, *J. Amer. Chem. Soc.*, 81, 4069 (1969).

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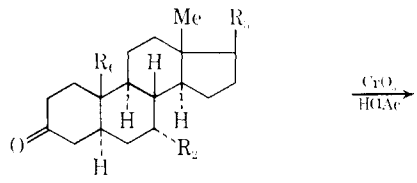
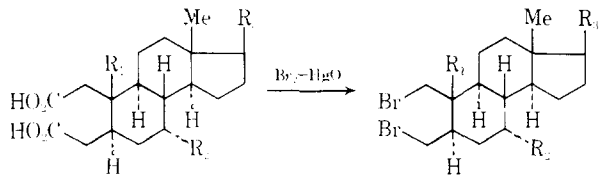
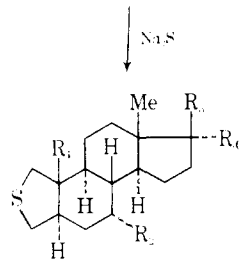
SCHEME I



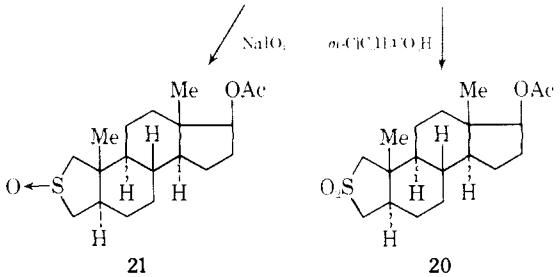
1. $R_1 = H$; $R_2 = H$; $R_3 = OAc$ (5α-H)
2. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OAc$ (5β-H)
3. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OH$ (5α-H)
4. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OAc$ (5α-H)



5. $R_1 = H$; $R_2 = H$; $R_3 = OAc$
6. $R_1 = CH_3$; $R_2 = H$; $R_3 = O$
7. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OAc$
8. $R_1 = H$; $R_2 = H$; $R_3 = OAc$
9. $R_1 = CH_3$; $R_2 = H$; $R_3 = O$
10. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OAc$



11. $R_1 = H$; $R_2 = H$; $R_3 = OH$; $R_4 = H$
12. $R_1 = CH_3$; $R_2 = H$; $R_3 = OH$; $R_4 = H$
13. $R_1 = CH_3$; $R_2 = H$; $R_3 = OAc$; $R_4 = H$
14. $R_1 = CH_3$; $R_2 = H$; $R_3 = R_4 = O$
15. $R_1 = CH_3$; $R_2 = H$; $R_3 = OH$; $R_4 = Me$
16. $R_1 = CH_3$; $R_2 = H$; $R_3 = OH$; $R_4 = Et$
17. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OH$; $R_4 = H$
18. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OAc$; $R_4 = H$
19. $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OCOCH_2CH_3$; $R_4 = H$



21 20

Oxidation of **4** with CrO_3–HOAc gave diacid **7**. Diacids **5**,[6] **6**,[7] and **7** were converted into dibromides **8**, **9**, and **10**, respectively, and thence to the thia steroids **11**, **14**, **17**, **18**, and **19** by the routes used previously[2] (see Scheme I). 17α-Alkyl derivatives **15** and **16** were obtained from **14** with MeMgBr or EtLi.

Discussion

Since the discovery of activity-enhancing groups in steroids, efforts have been made to quantitate the effects of these groups[8] and to explain their action. In doing this, it is necessary to consider a number of part processes in drug action[9] *viz.*, drug distribution and drug metabolism, drug–receptor affinity, and drug intrinsic activity. The importance of the drug metabolism part process is seen, for example, in the recent discoveries that 5α-dihydrotestosterone may be the active androgen in prostate tissue[10] and that the progestational 3-deoxy steroid 17α-ethyl-4-estren-17β-ol—a structure–function enigma—is metabolized by rat liver[11] to the well-known progestogen 17α-ethyl-19-nortestosterone. Therefore, although most structure–function theories concerning androgens and anabolic agents[12] consider only drug–receptor affinity, it is obvious that this represents a gross oversimplification of the problem, and one that is no doubt responsible for the wide variation in the theories thus far advanced. What is needed, therefore, is a type of molecular probe sufficiently different in structure from conventional androgens to allow the assumption that its metabolism, to the extent that it occurs at all, will be by pathways different from normal steroids. Similarly, the structure of the probe should differ enough from the conventional androgen to assure that a given molecular modification need not have an effect on drug distribution (*i.e.*, active or passive transport protein binding) common to both structural systems.

In the case of thia steroid **12** there is at hand, for the first time, an active compound sufficiently different in structure from conventional anabolic–androgenic compounds to justify such assumptions and to allow its use as such a probe. Thus, if a group like 7α-Me enhances activity in both the testosterone series *and* in the thia steroid series, it is reasonable to conclude that this effect is mediated at the receptor affinity–intrinsic activity level.

In the present work, we have examined the biological consequences of introducing a single Me group in three different areas of the steroid nucleus—at the 10β position, at the 7α position, and in going from a 17α-H to a 17α-Me substituent, and then from a 17α-Me to a 17α-Et substituent. In the 3-oxo-Δ^4 series, the results of these changes are well known—the removal of the C-19 Me group or the introduction of a 17α-Et group generally diminishes androgenic activity more than anabolic activity, whereas the introduction of a 7α-Me group enhances both activities.[13]

The data from the present pharmacological testing[14,15] are displayed in Table I.

It can be seen that sulfoxide **21** and sulfone **20** are devoid of activity. As these compounds are the most likely metabolites of thia steroid **12**, the activity of **12** is most reasonably attributed to the unmodified compound, and not to a metabolite.

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(7) P. M. Dvolaitzky, H. B. Kagan, and J. Jacques, *ibid.*, 598 (1961).
(8) For example, see J. Fried and A. Burman, *Vitam. Horm.* (New York), **16**, 303 (1959).
(9) E. J. Ariens, G. A. J. van Os, A. M. Simonis, and J. M. van Rossum, in "Molecular Pharmacology," E. J. Ariens, Ed., Academic Press, New York, N. Y., 1964, pp 4–5.
(10) N. Bruchovsky and J. D. Wilson, *J. Biol. Chem.*, **243**, 5963 (1968).
(11) H. Okada, M. Sumi, M. Ahara, and M. Ishihara, *Nippon Naibunpi Gakki Sasshi*, **44**, 1274 (1969). *Chem. Abstr.*, **71**, 109429 (1969).
(12) J. A. Vida, "Androgens and Anabolic Agents," Academic Press, New York, N. Y., 1969, pp 21–75.
(13) A full compilation of such data is given in ref 12.
(14) Pharmacological tests were performed at the Endocrine Laboratories, Madison, Wisc.
(15) L. G. Hershberger, E. G. Shipley, and R. K. Meyer, *Proc. Soc. Exp. Biol. Med.*, **83**, 175 (1953).

TABLE I
ANDROGENIC-MYOTROPHIC ASSAY

Compd (total dose, mg)	Wt, mg[a]			Body wt, g	
	Ventral prostate	Seminal vesicle	Levator ani	Initial	Final
Castrate control	15.8 ± 1.51	12.6 ± 1.21	25.2 ± 3.54	57	80
Testosterone propionate (0.3)	40.7 ± 5.47	15.3 ± 0.88	33.5 ± 3.17	57	90
p	<0.01	0.1	<0.2		
Testosterone (0.3)	30.2 ± 4.16	14.9 ± 0.77	31.3 ± 2.16	57	95
p	<0.02	<0.2	<0.2		
12 (3.0)[b]	61.9 ± 6.04	48.6 ± 3.56	65.2 ± 3.45	55	95
p	<0.001	<0.001	<0.001		
13 (3.0)[b]	46.9 ± 4.18	35.5 ± 3.06	56.8 ± 2.54	55	90
p	<0.001	<0.001	<0.001		
17 (3.0)	108.9 ± 9.29	78.2 ± 4.27	82.5 ± 4.01	57	99
p	<0.001	<0.001	<0.001		
18 (3.0)	105.4 ± 3.08	78.7 ± 3.16	74.2 ± 2.70	57	96
p	<0.001	<0.001	<0.001		
19 (3.0)	87.0 ± 5.94	69.7 ± 3.66	71.8 ± 2.65	57	95
p	<0.001	<0.001	<0.001		
15 (3.0)	73.4 ± 4.87	44.2 ± 2.25	65.4 ± 3.64	57	97
p	<0.001	<0.001	<0.001		
16 (2.4)	25.1 ± 5.90	14.4 ± 0.47	39.7 ± 1.02	57	95
p	<0.2	*ca.* 0.2	<0.01		
11 (3.0)	32.6 ± 1.75	28.7 ± 2.11	57.9 ± 1.55	57	100
p	<0.001	<0.001	<0.001		

[a] Mean ± standard error. [b] See ref 16.

The changes produced in the activities of the remaining compounds in Table I by the various enhancing groups closely parallel the corresponding changes found in the testosterone series. Thus, removal of the 19-angular Me (**11**) results in enhancement of the anabolic–androgenic ratio and a decline in overall potency. Introduction of a 17α-Me (**15**) raises ventral prostate activity slightly but has rather little effect generally. By contrast, introduction of 17α-Et (**16**) causes a sharp reduction in androgenic potency and a lesser loss of anabolic activity, in harmony with results found in the testosterone series. Finally, the 7α-Me compounds **17**, **18**, and **19** show an extremely interesting pattern of activity. Free alcohol **17** and acetate **18** are the most potent anabolic and androgenic thia steroids tested to date, again paralleling the effect of this modification in the testosterone series. Propionate **19** is less active.[16] It is of interest that the activating influence of the ester groups is not followed in the thia steroid series. The ester group is now known[17] to influence the rate of release of testosterone esters from body fats through an influence on the partition coefficient. Since the partition coefficient of **17** may well be different from testosterone, it is not unanticipated that propionate **19** could be less active than alcohol **17**. This is an example of the *nonparallelism* in the two series which would be expected for modifications affecting drug distribution or drug metabolism. All the data, therefore, are consistent with the notion that the 19-Me, 7α-Me, and 17α-Me groups affect drug–receptor interactions. The effects of some of these groups are through direct interaction with the receptor, in terms of the working hypothesis of the steroid receptor complex used in this laboratory.[18] Thus, changes in activity due to modification of substituents at C-10 or C-17α are mediated through interaction of these groups with the receptor surfaces in contact with the β face and α face, respectively, of the steroid. On the other hand, the effect produced by the 7α substituent is most probably due to a change produced in the conformation of the steroid itself, through conformational transmission.[19] The axial 7α substituent is involved in repulsive interactions with the 5α, 9α, and 14α protons. Therefore, the effect of this substituent would be to flatten the molecule toward the β face. This flattening effect has been demonstrated by X-ray measurements in the case of the 9α-halogen compounds, in which the 9α substituent interacts similarly with protons at the 1α, 5α, 7α, and 14α positions.[20]

(16) Through an error in ref 2, the activities of acetate 13 were interchanged with free alcohol 12. The correct figures are given in this paper; free alcohol 12 is the more active of the two compounds.

(17) K. C. James, P. J. Nicholls, and M. Roberts, *J. Pharm. Pharmacol.*, **21**, 24 (1969).

Experimental Section[21]

7α-Methyl-17β-hydroxyandrost-4-en-3-one.—To an ice-cold solution of MeMgBr (100 ml; 3 *M* in Et_2O) was added anhyd THF (200 ml) with stirring followed by anhyd Cu_2Cl_2 (1.7 g). A solution of 6-dehydrotestosterone (10 g) in THF (250 ml) was added in a thin stream. The mixture was allowed to come to

(18) M. E. Wolff, W. Ho, and R. Kwok, *J. Med. Chem.*, **7**, 577 (1965).

(19) D. H. R. Barton, A. J. Head, and P. J. May, *J. Chem. Soc.*, 935 (1957).

(20) A. Cooper, C. T. Lu, and D. A. Norton, *ibid.*, 1228 (1968).

(21) Melting points were determined with a Thomas–Hoover apparatus equipped with a corrected thermometer. Microanalyses were performed by the Microanalytical Department, University of California, Berkeley Calif. Nmr spectra were obtained at 60 MHz on samples of $CDCl_3$ on a Varian A-60A instrument or at 100 MHz on a Jeolco JMH-100 instrument using TMS as internal standard. Mass spectra were obtained by Mr. William Garland on a MS-902 high-resolution instrument. ORD-CD measurements were made by Dr. H. H. Chang with a Jasco ORD/UV-5 apparatus. Optical rotations were obtained in a 0.5-dm tube with a Rudolph photoelectric polarimeter. Where analyses are indicated only by symbols of the elements or functions, analytical results obtained for those elements or functions were within ±0.4% of the theoretical values.

room temp and then refluxed gently for 4 hr. It was kept at 24° overnight and poured over ice–dil HCl satd with NaCl in the presence of Et_2O (250 ml). The organic layer was sepd and the aq layer was extracted with Et_2O. The Et_2O extracts were washed with satd NaCl solution, dil NaOH solution, satd NaCl solution, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was crystallized from Me_2CO to give 4.1 g of pure product, mp 213–215° (lit.[3] 211–214°).

7α-Methyl-17β-hydroxy-5β-androstan-3-one 17-Acetate (2).—7α-Methyl-17β-hydroxyandrost-4-en-3-one (0.4 g) in EtOH (30 ml) was hydrogenated in the presence of PtO_2 (50 mg) at 24°. When the calcd amount of H_2 was absorbed, the catalyst was filtered, the EtOH was removed under reduced pressure, and the dried residue was acetylated with C_5H_5N (5 ml) and Ac_2O (2 ml). After 18 hr the reaction mixture was poured into H_2O and the ppt collected, washed with H_2O, and dried. Recrystallization from hexane gave 0.32 g of crystals: mp 151–152°; RD (*c*, 0.4 C_2H_5OH), 20°; $[\phi]_{340}$ −187°; $[\phi]_{307}$ −520°; $[\phi]_{299}$ 0°; $[\phi]_{276}$ +475°; CD $[\theta]_{325}$ 0; $[\theta]_{292}$ −2229; $[\theta]_{255}$ 0. Use of Pd–C (10%) catalyst under the above conditions resulted in a mixture of 5α and 5β isomers. The analytical sample was crystallized from hexane, mp 151–152°. *Anal.* ($C_{22}H_{34}O_3$) C, H.

7α-Methyl-17β-hydroxy-5α-androstan-3-one (3).—A solution of 7α-methyl-17β-hydroxyandrost-4-en-3-one (8 g) in a mixture of dry dioxane (180 ml) and anhyd Et_2O (180 ml) was added slowly to a solution of Li (1 g) in anhyd liquid NH_3 (800 ml) with efficient stirring. The mixture was stirred for 10 min and then decomposed with solid NH_4Cl (8 g). NH_3 was allowed to evap overnight and the residue was treated with H_2O and extd with $CHCl_3$. The $CHCl_3$ extract was washed with H_2O and dried (Na_2SO_4), and the dry residue was crystallized from hexane to give 6 g of **3**, mp 192–194°. The analytical sample was crystallized from Me_2CO: mp 193–194°; $[\alpha]^{20}D$ +10° (*c*, 1 $CHCl_3$). *Anal.* ($C_{20}H_{32}O_2$) C, H,

7α-Methyl-17β-hydroxy-5α-androstan-3-one 17-Acetate (4).—Compound **3** (6 g) was acetylated with C_5H_5N (50 ml) and Ac_2O (10 ml). The reaction mixture was allowed to stand at room temp overnight. The residue from the work-up by Et_2O extn was crystallized from a hexane–Me_2CO mixture to give 6 g of product: mp 140–141°; RD (*c*, 0.4 C_2H_5OH), 20°; $[\phi]_{336}$ +87°, $[\phi]_{306}$ +850°, $[\phi]_{284}$ 0°, $[\phi]_{278}$ −150°, $[\phi]_{268}$ 0°; CD $[\theta]_{289}$ +2858. *Anal.* ($C_{22}H_{34}O_3$) C, H.

7α-Methyl-17β-hydroxy-2,3-seco-5α-androstane-2,3-dioic Acid 17-Acetate (7).—To a stirred solution of **4** (2 g) in glacial HOAc (40 ml) at 50° was added a solution of CrO_3 (2 g) in H_2O (6 ml) and HOAc (6 ml). It was stirred for 6 hr at 58–60° and kept overnight at room temp. The solution was poured into ice–H_2O satd with NaCl and the ppt was collected and washed with H_2O. The pale greenish white solid was taken up in $NaHCO_3$ solution and the mixture was washed with Et_2O. The combined Et_2O washings were extd once with aq $NaHCO_3$ solution. The combined $NaHCO_3$ solution was cooled, satd with NaCl, and acidified with concd HCl. The white ppt was collected, washed with H_2O, and dried to give 1.5 g of powder. It was recrystd from aq MeOH to give colorless crystals (0.9 g): mp 283–285°; $[\alpha]^{20}D$ −12° (*c* 1, 95% EtOH). *Anal.* ($C_{22}H_{34}O_6$) C, H.

1,4-Dibromo-1,4-seco-2,3-bisnor-5α-estran-17β-ol Acetate (8).—This compd was made from **6** in a manner similar to that described for the preparation of **9**. The product was obtained by chromatography on silica gel using 0.5–5.0% Me_2Co in petr ether for elution, followed by recrystn from aq MeOH to furnish 0.325 g of colorless crystals: mp 140–142°; $[\alpha]^{20}D$ +17° (*c* 1, EtOH). *Anal.* ($C_{18}H_{28}Br_2O_2$) C, H, Br.

1,4-Dibromo-1,4-seco-2,3-bisnor-5α-androstan-17-one (9).—To 1.8 g of **6**[7] in 100 ml of stirred refluxing CCl_4, there was added 1.6 g of red HgO. The reaction mixture was shielded from light, and Br_2 (1.6 g) was added dropwise. After 3 hr the reaction mixture was allowed to cool. It was filtered and the filtrate was concd under vacuum. The residue was chromatographed on Al_2O_3 to give 0.8 g of pure **9** which was recrystd from MeOH: mp 149–150°; $[\alpha]^{20}D$ +48° (*c* 1, $CHCl_3$). *Anal.* ($C_{17}H_{26}Br_2O$) C, H, Br.

7α-Methyl-1,4-dibromo-1,4-seco-2,3-bisnor-5α-androstan-17β-ol Acetate (10).—This compd was prepared in a manner similar to that used for the preparation of **9**. The product was obtained by chromatography on silica gel using 10% EtOAc in hexane as eluent and after recrystn from EtOH had mp 147–148°, $[\alpha]^{20}D$ −22° (*c* 1, $CHCl_3$). *Anal.* ($C_{20}H_{32}Br_2O_2$) C, H.

2-Thia-A-nor-5α-estran-17β-ol (11).—To a refluxing solution of 0.3 g of **8** in 50 ml of EtOH, there was added a tenfold excess of Na_2S dissolved in the minimum amount of H_2O. The reaction mixture was refluxed for 16 hr, at which time tlc indicated complete conversion of the dibromide into product. The solvent was distd and the white residue was dissolved in Et_2O, washed with H_2O, and dried (Na_2SO_4). The solvent was removed under vacuum and the residue was recrystd from MeCN to afford 0.15 g of product: mp 165–166°; $[\alpha]^{20}D$ +78° (*c* 1, EtOH). *Anal.* ($C_{16}H_{26}OS$) C, H, S.

2-Thia-A-nor-5α-androstan-17-one (14). Procedure A.—A solution containing 0.15 g of **12**, 6 ml of cyclohexanone, and 0.3 g of $Al(i\text{-}OPr)_3$ in 300 ml of PhMe was heated under reflux for 2.5 hr, cooled, and evapd under reduced pressure. The residue was taken up in Et_2O, washed with H_2O, and steam distd to afford an aq suspension which was extd with Et_2O. Removal of the Et_2O under vacuum gave a residue which was adsorbed on silica gel and eluted with 2% EtOH in C_6H_6. The product was recrystd from MeOH to give 0.04 g of pure sample: mp 140–142°; $[\alpha]^{20}D$ +160° (*c* 1, $CHCl_3$). *Anal.* ($C_{17}H_{26}OS$) C, H, S.

Procedure B.—The product was obtained from **9** by the method described for the preparation of **11**, and had mp 140–141°.

17α-Methyl-2-thia-A-nor-5α-androstan-17β-ol (15).—To a solution of 0.1 g of **14** in 20 ml of Et_2O was added 3 ml of 3 *M* MeMgBr in Et_2O. The mixture was refluxed for 5 hr when tlc showed the reaction was complete. The mixture was poured onto ice and acidified with 10% HCl. The Et_2O layer was sepd and the aq layer was extd once with 150 ml of Et_2O. The Et_2O extract was washed with 5% $NaHCO_3$ solution and H_2O and dried (Na_2SO_4). Evaporation of the solvent yielded a solid which was chromatographed on silica gel to give 0.06 g of white solid, which when recrystd from MeOH had mp 139–140°, m^+ 294, $[\alpha]^{20}D$ +38° (*c* 1, $CHCl_3$). *Anal.* ($C_{18}H_{30}OS$) C, H, S.

17α-Ethyl-2-thia-A-nor-5α-androstan-17β-ol (16).—A solution of 0.1 g of **14** in 10 ml of THF was added dropwise under N_2 to 10 ml of 1.29 *M* EtLi in C_6H_6. The mixture was stirred at 0° for 2 hr, and an additional 5 ml of EtLi reagent was added. After 15 min the mixture was poured onto ice containing dil HCl, the Et_2O layer was sepd, and the aq phase was extracted twice with Et_2O. The combined Et_2O extracts were washed with dil HCl, $NaHCO_3$ solution, and H_2O, and dried (Na_2SO_4). Evapn of the solvent yielded 0.08 g of a solid mixture which was sepd on preparative tlc using hexane–Me_2CO to give 0.04 g of product, which was then recrystd from MeOH to give the anal sample of mp 141–142°; m^+ 308. *Anal.* ($C_{19}H_{32}OS$) C, H.

7α-Methyl-2-thia-A-nor-5α-androstan-17β-ol (17) was obtained from **10** by the method described for the preparation of **11**. Crystallization from hexane gave feathery crystals (0.2 g): mp 152–154°; $[\alpha]^{20}D$ +14° (*c* 1, $CHCl_3$). *Anal.* ($C_{18}H_{30}OS$) C, H.

7α-Methyl-2-thia-A-nor-5α-androstan-17β-ol Acetate (18).—Compound **17** (0.075 g), in C_5H_5N (3 ml), was acetylated with Ac_2O (1 ml) and kept at room temp for 2 days. The product was isolated with Et_2O and was crystallized from hexane to give fine needles: mp 122–123°; $[\alpha]^{20}D$ +120° (*c* 1, $CHCl_3$). *Anal.* ($C_{20}H_{32}O_2S$) C, H.

7α-Methyl-2-thia-A-nor-5α-androstan-17β-ol Propionate (19).—A solution of **17** (0.05 g) in C_5H_5N (2 ml) was treated with $(EtCO)_2O$ (1 ml) and kept at room temp overnight. The solid isolated by extraction with Et_2O was chromatographed over silica gel. Elution with petr ether–EtOAc (39:1) gave **19** (0.045) which was crystallized from petr ether to give needle-like crystals: mp 88–90°; $[\alpha]^{20}D$ +16° (*c* 1, $CHCl_3$). *Anal.* ($C_{21}H_{34}O_2S$) C, H.

17β-Hydroxy-2-thia-A-nor-5α-androstane-2,2-dioxide Acetate (20).—To a solution of 0.1 g of **13** in 30 ml of C_6H_6 there was added 0.3 g of *m*-$ClC_6H_4CO_3H$, and the reaction mixture was stirred for 2 hr. The reduced reagent was removed by filtration and the filtrate was washed several times with satd aq $NaHCO_3$ in order to remove excess peracid. The C_6H_6 layer was concd to dryness by distillation under reduced pressure and the residual crude product was purified by crystallization from Me_2CO–C_6H_6 hexane, giving 0.08 g of pure **20**: mp 243–244°; m^+ 354 $[\alpha]^{20}D$ +280° (*c* 1, $CHCl_3$). *Anal.* ($C_{19}H_{30}O_4S$) C, H, S.

17β-Hydroxy-2-thia-A-nor-5α-androstan-2-oxide Acetate (21).—To a solution of 0.1 g of **13** in 20 ml of Me_2CO and 1 ml of H_2O there was added portionwise 0.05 g of $NaIO_4$ and the reaction mixture was stirred for 24 hr at 24°. The Me_2CO was evapd under reduced pressure, the residue was taken up in Et_2O, washed with H_2O, and evapd under reduced pressure. The residue was then crystallized several times from hexane–Et_2O to give 0.07 g of pure product: mp 139–140°; m^+ 338 $[\alpha]^{20}D$ +68° (*c* 1, $CHCl_3$). *Anal.* ($C_{19}H_{30}O_3S$) C, H, S.