21.2 g. of 19-norandrostane-3,17-dione (I, m.p. 74.5–76.5°, $[\alpha]_D^{27}$ +132° (acetone)) in 1000 ml. of methanol. The mixture was allowed to stand at 20° for 30 min. and the reaction was stopped with dilute sulfuric acid. The reduction products were extracted with ethyl acetate and washed with water, dilute base, and 10% sodium chloride solution. The ethyl acetate solution was dried and the solvent evaporated to yield 18.8 g. of oily product. Chromatography on 2 kg. of silica gel with ethyl acetate–petroleum ether (b.p. 30–60°) (3:1) afforded 10.6 g. of 3β-hydroxy-19-norandrostane-17-one (IIa) contaminated with a small amount of the 3α-hydroxy epimer. Recrystallizations from acetone yielded 5.64 g. of IIa, m.p. 179–180.5°. The analytical sample of 3β-hydroxy-19-norandrostane-17-one melted at 180–180.5°; $[\alpha]_D^{26}$ +106°; reported[7] m.p. 177–179°, $[\alpha]_D^{20}$ +108°; ν_{max} 3622, 1743, and 1408 cm.$^{-1}$

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.17; H, 9.57.

Acetylation of IIa with acetic anhydride and pyridine at room temperature yielded 3β-acetoxy-19-norandrostane-17-one (IIb). Recrystallizations from methanol yielded IIb, m.p. 182.5°; $[\alpha]_D^{26}$ +80.3°; ν_{max} 1743, 1737(sh), 1408, and 1245 cm.$^{-1}$

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.26; H, 9.54.

Further elution of the column with ethyl acetate–petroleum ether (3:1) yielded 5.24 g. of 19-norandrostane-3,17-diols. Recrystallizations of a small portion afforded 19-norandrostane-3β,17β-diol (IIIa), m.p. 174.5–175.5°; $[\alpha]_D^{26}$ +26.3° (ethanol); reported[8] m.p. 168–170°; $[\alpha]_D$ +37°. Acetylation of IIIa with acetic anhydride and pyridine at room temperature afforded the diacetate IIIb, m.p. 144–144.5°; $[\alpha]_D^{27}$ +3.2°; reported[9] m.p. 140.2–141.8°; $[\alpha]_D^{25}$ +4.4°.

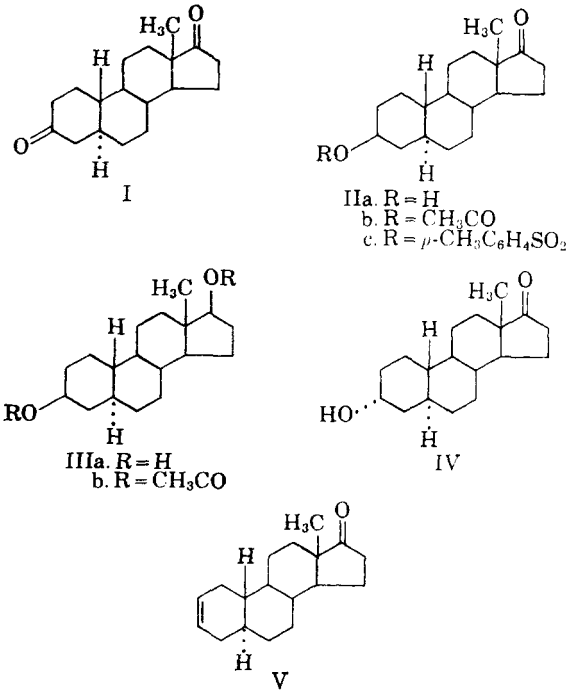
3β-p-Toluenesulfonoxy-19-norandrostane-17-one (IIc). A cold solution of 370 mg. of *p*-toluenesulfonyl chloride in 1 ml. of pyridine was added to a solution of 250 mg. of 3β-hydroxy-19-norandrostane-17-one (IIa) in 2 ml. of pyridine. The reaction mixture was allowed to stand overnight at room temperature and worked up in the usual manner. The product was recrystallized from acetone to yield 251 mg. of 3β-*p*-toluenesulfonoxy-19-norandrostane-17-one (IIc), m.p. 152–154.5° (dec.); $[\alpha]_D^{26}$ +55.9°.

Anal. Calcd. for $C_{25}H_{34}O_{11}$ S: C, 69.73; H, 7.96. Found: C, 69.78; H, 7.91.

3α-Hydroxy-19-norandrostane-17-one (IV). The crude tosylate IIc obtained from 5.28 g. of 3β-hydroxy-19-norandrostane-17-one and 7.3 g. of *p*-toluenesulfonyl chloride was dissolved in 220 ml. of *N,N*-dimethylformamide and the solution was kept at 80–85° for 68 hr. Large volumes of ice and water were added to the cooled reaction mixture. The product was extracted with ethyl acetate and washed with water. The ethyl acetate solution was dried over sodium sulfate and the solvent evaporated to yield 5.4 g. of dark brown oil. The residue was refluxed for 1 hr. with 20 g. of potassium hydroxide in 400 ml. of methanol and 45 ml. of water and the product was worked up in the usual manner to give 4.3 g. of oil. This was chromatographed on 160 g. of acid washed alumina. Elution with benzene–petroleum ether (1:3) afforded 1.87 g. of 19-nor-Δ^2-androstene-17-one (V). Recrystallizations from acetone–petroleum ether and methanol yielded V, m.p. 123.5–124.5°; $[\alpha]_D^{28}$ +170°; ν_{max} 1743, 1658, and 1408 cm.$^{-1}$ A small amount of contamination with 19-nor-Δ^2-androstene-17-one was detected by absorption at 1647 cm.$^{-1}$

Anal. Calcd. for $C_{18}H_{26}O$: C, 83.67; H, 10.14. Found: C, 83.44; H, 9.96.

Further elution of the column with mixtures of ethyl acetate–benzene yielded 2.47 g. of 3α-hydroxy-19-norandrostane-17-one (IV). Recrystallizations from acetone–petroleum ether yielded 1.60 g. of fine needles of IV, m.p. 157.5–160° with change of crystalline form at 144°; $[\alpha]_D^{32}$ +110° Upon drying *in vacuo* at 100° for 2 hr., it melted at 164–165°. The analytical sample of 3α-hydroxy-19-norandrostane-17-one recrystallized from acetone melted at 167–168°; $[\alpha]_D^{27}$ +114°; ν_{max} 3615, 1743, and 1408 cm.$^{-1}$ The sample of 3α-hydroxy-19-norandrostane-17-one obtained from Dr. L. L. Engel melted in our laboratory at 158–161° with change in crystal form at 144°, reported m.p. 153–156°; $[\alpha]_D^{26}$ +103°. Upon heating *in vacuo* at 100° for 2 hr., it melted at 160–162°; changes in crystal form at 143°. The melting point of the synthetic sample of IV was not depressed upon admixture with the urinary steroid.[4] The infrared spectra of the two samples were identical.



Acknowledgment. The authors gratefully acknowledge the support and interest of Dr. T. F. Gallagher throughout this investigation. We wish to express our appreciation to Mrs. Beatrice S. Gallagher for the determination and interpretation of the infrared spectra and to the Upjohn Co., Kalamazoo, Mich., for a generous supply of 19-nortestosterone.

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Hydrogenolysis of Thioesters

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Received December 29, 1960

Since the work of Nystrom and Brown,[2] the hydrogenolysis of esters by lithium aluminum hydride has been successfully applied to a wide

variety of esters but apparently no similar reaction has been reported for thiolesters. In the latter case the milder reaction conditions prevailing in hydrogenolysis over hydrolysis could be favorable to a better yield of mercaptan. This has been now demonstrated in the case of acyl derivatives of mercaptosterols.

From the hydrogenolysis of thioesters both the alcohol corresponding to the acyl group and the free mercaptan could be isolated and identified, accounting for 95–98% of the reaction products. Dioxane and ether are suitable solvents for the hydrogenolysis which can be carried out at room temperature or sped up by heating the reagents. When the reaction is carried out at semimicro level separation and purification of the mercaptans was best accomplished through the corresponding lead mercaptides.

Although esters are generally resistant to sodium borohydride,[3] phenyl thiobenzoate gave a 40% yield of thiophenol when the thioester was reduced with sodium borohydride in dioxane. In *n*-butyl ether the thioester was quantitatively recovered unchanged.

Cholestanyl thiobenzoate afforded 3-mercaptocholestane in 50% yield by hydrolysis with sodium ethoxide; resinous material which formed in the reaction made it difficult to crystallize the thiol. However a 65% yield and practically no resinous material was obtained by the use of lithium aluminum hydride.

The pertinent results are summarized in Table I.

TABLE I

REDUCTION OF THIO ESTERS BY $LiAlH_4$

Thio ester	Solvent	Thiol Formed	Yield of Thiol, %
n-Butyl thiobenzoate	$(C_2H_5)_2O$	*n*-Butyl mercaptan	45
2-CH_3-propanethiol benzoate	$(C_2H_5)_2O$	2-Methylpropanethiol	44
2-CH_3-2-propanethiol benzoate	$(C_2H_5)_2O$	2-Methyl-2-propanethiol	41
Phenyl thiobenzoate	Dioxane	Thiophenol	96
Benzyl thiobenzoate	$(C_2H_5)_2O$	Benzyl mercaptan	85
p-CH_3O-benzyl thiobenzoate	Dioxane	*p*-Methoxy benzyl mercaptan	96
7-Thioacetylcholesteryl benzoate	$(C_2H_5)_2O$	7-Mercaptocholesterol	83
Cholestanyl thiobenzoate	$(C_2H_5)_2O$	3-Mercaptocholestane	65

(1) This work is taken from part of a thesis directed by the late Prof. Heinrich Hauptmann and submitted by Paulo A. Bobbio to the Univ. of S. Paulo in partial fulfillment of the requirements for the Doctor of Science degree.

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EXPERIMENTAL

All thioesters used were purified by fractional distillation or recrystallization. A typical example of the hydrogenolysis is as follows:

A solution of 14.0 g. of benzyl thiobenzoate in 50 ml. of ether was slowly added to a mechanically stirred suspension of 3.0 g. of lithium aluminum hydride in 250 ml. of ether. After 5 hr. the excess of lithium aluminum hydride was destroyed with hydrochloric acid. The ether layer was washed and dried and, after elimination of the solvent, the residue was fractionally distilled. Yield of benzyl mercaptan, b.p. 192–194°, 6.5 g.

Acknowledgment. We are indebted to the Rockefeller Foundation, to "CAPES," and the Brazilian "Conselho Nacional de Pesquisas" for grants.

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3-Mercapto-2,2-diethyl-1-propanol. Opening of Oxetane Rings by Sulfur-Containing Nucleophilic Reagents

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Received November 10, 1960

2,2-Disubstituted 3-mercapto-1-propanols were desired for conversion to 5,5-disubstituted 1,3-oxathianes by reaction with carbonyl compounds.[1] Mercaptopropanols $HSCH_2CR_2CH_2OH$ appear to be unknown. Several possible synthetic methods were investigated briefly. Displacement of the bromide atom in I by thiourea in ethanol, either at 80° or 150°, yielded only traces of the mercapto alcohol III, a result not unexpected from the known unreactivity of neopentyl-type halides.

$$BrCH_2CR_2CH_2OAc + HSC(=NH)NH_2 \longrightarrow$$

I. R = CH_3
II. R = C_2H_5

$$\left[H_2N(NH_2{=})CSCH_2CR_2CH_2OAc \right]^{+}\ Br^- \xrightarrow{\text{base}} HSCH_2CR_2CH_2OH$$

III. R = CH_3
IV. R = C_2H_5

Ring opening of 3,3-diethyloxetane by sulfur-containing nucleophiles was then examined. The oxetane ring is known to undergo displacement with nucleophiles much like the more familiar oxiranes, though less readily. For example, Searles[2] has explored the reaction of oxetane itself with mercaptans and with thiosulfate ion. Sodium sulfide, even in large excess, converted oxetane into the sulfide, not the mercaptan.[2] Substituted oxetanes are

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(2) S. Searles, *J. Am. Chem. Soc.*, **73**, 4515 (1951). The Bunte salt was not isolated.