At the ED_{50} in the rotating rod test, the duration of activity was determined to be about 15 min.

(Hydroxymethyl)benzyldimethylsilane Carbamate.—(Chloromethyl)benzyldimethylsilane, bp 89–90° (4 mm), $n^{29}D$ 1.5175, was prepared in 74% yield from 100 g (0.70 mole) of (chloromethyl)dimethylchlorosilane and 1.1 moles of benzylmagnesium chloride.

Anal. Calcd for $C_{10}H_{16}ClSi$: Si, 14.05. Found: Si, 14.18.

From 65 g (0.32 mole) of the (chloromethyl)silane, there was obtained 65.5 g (90%) of the acetate, bp 108° (2.0 mm), $n^{26}D$ 1.4972.

Anal. Calcd for $C_{12}H_{18}O_2Si$: Si, 12.62. Found: Si, 12.71.

The preparation of the hydroxymethylsilane was accomplished by hydrolysis.[6] To 39.3 g (0.18 mole) of the acetate was added 300 ml of aqueous methanol and 4 drops of concentrated H_2SO_4. The mixture was heated at reflux for 24 hr. Fractional distillation gave 28.8 g (90%) of the crude material. After repeated distillation, an analytical sample was obtained.

Anal. Calcd for $C_{10}H_{16}OSi$: Si, 15.55. Found: Si, 15.37.

Using 18.9 g (0.105 mole) of the hydroxymethyl compound, the carbamate, bp 170° (5.5 mm), $n^{25}D$ 1.5240, was obtained in 43% yield. The product solidified, and crystallization from acetone yielded 5.3 g, mp 65–66°.

Anal. Calcd for $C_{11}H_{17}NO_2Si$: C, 59.14; H, 7.69; Si, 12.57. Found: C, 59.30; H, 7.5; Si, 12.63.

The LD_{50} of this carbamate was found to be greater than 1000 mg/kg; the ED_{50} for the rotating rod was 318 (294–344) mg/kg. The duration of activity was observed to be 10 min at the ED_{50} level.

Hydroxymethylphenethyldimethylsilane Carbamate.—(Chloromethyl)phenethyldimethylsilane, bp 113–115° (5 mm), $n^{25}D$ 1.5100, was obtained in 50% yield from phenethylmagnesium bromide and (chloromethyl)dimethylchlorosilane. No attempt was made to obtain an analytical sample. From 70.1 g (0.046 mole) of the (chloromethyl)silane, there was obtained 70.4 g (90%) of the acetate, bp 128–130° (4.2 mm), $n^{24}D$ 1.4939.

Anal. Calcd for $C_{13}H_{20}Si$: Si, 11.87. Found: Si, 11.88.

Hydrolysis[6] of 43.4 g (0.19 mole) of the acetate yielded 18.4 g (50%) of the crude (hydroxymethyl)silane. Repeated redistillations gave a pure sample, bp 130–131° (6 mm), $n^{23}D$ 1.5141.

Anal. Calcd for $C_{11}H_{18}OSi$: Si, 14.41. Found: Si, 14.27.

From 10.7 g (0.058 mole) of the (hydroxymethyl)silane was obtained 7.7 g (58%) of the carbamate, bp 174–176° (4 mm), $n^{23}D$ 1.5170. When chilled, the carbamate solidified; mp 36–37°.

Anal. Calcd for $C_{12}H_{19}NO_2Si$: C, 60.70; H, 8.09; N, 5.90; Si, 11.82. Found: C, 60.70; H, 7.94; N, 5.85; Si, 11.98.

The infrared spectrum, consistent with the expected structure, showed a doublet in the 2.9-μ region and the expected bands at 5.7, 6.23, 8.0, and 9.4 μ.

The LD_{50} was observed to be greater than 1000 mg/kg; the ED_{50} for the rotating rod was 308 (290–326) mg/kg. The duration of activity at the ED_{50} level was 20 min.

Acknowledgment.—The authors are indebted to Mr. J. Dias for aid in the synthetic work.

(6) It should be noted that this procedure, which is in deviance with our usual procedure of reduction, gave inferior results when the purity of the product and the difficulty in obtaining an analytical sample are considered. Although never applied to the preparation of this particular compound, the authors consider the $LiAlH_4$ reduction procedure superior to this method.

Isomeric Estranes

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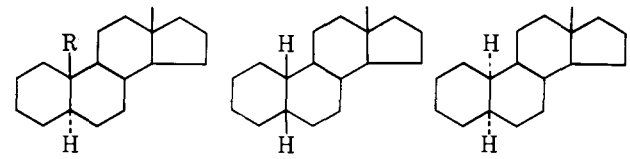
In 1960, Segaloff and Gabbard[2] demonstrated that 5α-androstane (Ib) was able to stimulate the seminal vesicles and prostate of the castrated rat. This indicated that oxygenated funtions at the 3- and 17-positions of androstanes was not obligatory for androgenic activity. For spectroscopic reasons, 5α-estrane (Ia), the 19-nor analog of Ib, as well as 5β- (II) and 5α,10α-estrane (III) have now been prepared. These isomers were readily obtained by Wolff–Kishner reduction of the previously described 3,17-diketones.[3] Intramuscular administration of Ia in castrated male rats showed it to have less than 1% of the androgenic activity of testosterone propionate.[4]



Ia, R = H
b, R = CH_3 II III

Experimental Section[5]

5α-Estrane (Ia). General Method.—A solution of 5α-estrane-3,17-dione[3] (2.7 g), 100% hydrazine hydrate (3 ml), and KOH pellets (2.0 g) in diethylene glycol (20 ml) was refluxed for 1 hr. The condenser was removed and the external temperature was raised. A stream of nitrogen was passed into the vessel for 20 min. The external temperature was raised to 230° and the mixture refluxed for 2 hr. The solution was allowed to cool and was poured into ice water (100 ml). The mixture was extracted with three 50-ml portions of ether and the extract was washed successively with two 25-ml portions of 2 *N* HCl and water (25 ml). The ether phase was dried (Na_2SO_4 and Darco) and the solvent was removed by distillation. The residual oil (1.6 g) was distilled *in vacuo* to afford pure Ia (see Table I).

TABLE I

Estrane	Bp, °C (mm)	$[\alpha]^{25}D$, deg	$n^{25}D$	18-H, δ (ppm)	% found[a] C	H
5α	133–135(4)	+20	1.517	0.692	88.22	12.19
5β	102–103 (0.05)	+15	1.514	0.700	87.63	12.02
5α,10α	83–85(0.03)	−15.5	1.524	0.675	87.95	12.42

[a] *Anal.* Calcd for $C_{18}H_{30}$: C, 87.73; H, 12.27.

(3) R. E. Counsell, *Tetrahedron*, **15**, 202 (1961).

(4) The author is grateful to Dr. F. J. Saunders for providing the biological information.

(5) Optical Rotations and analytical data were furnished by Dr. R. T. Dillon of our Analytical Department. The optical rotations were obtained in $CHCl_3$. The nmr spectra were obtained in $CDCl_3$ with a Varian high-resolution Model V-4300B using tetramethylsilane as the internal standard. These spectra were kindly provided by Dr. McNiven, Worcester Foundation for Experimental Biology.

Synthesis of Arysulfonyl-1-methyl-S-isothiosemicarbazides

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Lora-Tamayo,[1] *et al.*, and Hoggarth[2] have reported syntheses of a number of aroyl-1-methyl-S-isothiosemicarbazides. These compounds, as well as the related aroylthiosemicarbazides, show antimicrobial activity. The preparation of the bioisosteric arylsulfonyl-1-methyl-S-isothiosemicarbazides (I) from the corresponding arylsulfonylthiosemicarbazides is given here as a further utilization of the latter compounds, whose preparation and evaluation were reported[3] elsewhere. While the experi-

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