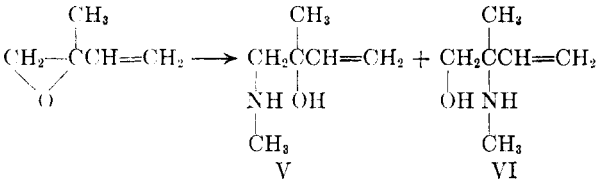
This is somewhat surprising in view of the recent report[6] that the reaction of 3,4-epoxy-3-methyl-1-butene with methylamine gave a mixture of the primary (V) and secondary (VI) addition products in the ratio of 10 to 1. The addition of ethylenimine to 1,2-epoxybutane followed by distillation of the product, gave a 50% yield of a material which was 98% pure as shown by vapor phase chromatography and which is presumed to be β-(1-aziridinyl)-α-ethylethanol (III). Similarily, 2,3-epoxybutane gave a 45% yield of β-(1-aziridinyl)-α,β-dimethylethanol (IV) which was 93% pure according to vapor phase chromatography.



V VI

EXPERIMENTAL[7]

3,4-Epoxy-3-methyl-1-butene. To a vigorously stirred suspension of 67.3 g. (0.99 mole) of isoprene in 250 ml. of water was added 176.1 g. (0.99 mole) of *N*-bromosuccinimide at a rate which kept the temperature between 18–25°. After the addition (about 0.5 hr.) was complete, the mixture was stirred at 18–25° for 2–3 hr. by which time all of the *N*-bromosuccinimide was in solution and the solution gave a negative test with potassium iodide paper.

The organic layer was extracted with three 90-ml. portions of diethyl ether. The combined ether layers were dried over magnesium sulfate, then evaporated to dryness *in vacuo* to yield 151 g. of the crude bromohydrin of isoprene.

The isoprene bromohydrin was added over 20–30 min. to 270 g. of 30% aqueous sodium hydroxide which had been cooled to 10–15° in an ice bath. After the addition was complete, the reaction was stirred at about 10° for 2 hr., then the organic phase was separated from the aqueous layer. The aqueous layer was washed with 50 ml. of ether. The ether layer and organic layer were combined, dried over magnesium sulfate, then distilled through a small Vigreux column to yield 33.7 g. (41%) of 3,4-epoxy-3-methyl-1-butene, b.p. 78–82°, n_D^{26} 1.4139, which was 91% pure as shown by vapor phase chromatography;[8] $\lambda_{max(\mu)}^{film}$ 6.07 (C=C), 7.20 (CH_3), 10.08, 10.85 (—CH=CH_2), 11.25, 12.75 (epoxide).

Pummerer and Reindel[9] prepared this compound in 30–40% yield by the reaction of isoprene with perbenzoic acid. They reported b.p. 81° (735 mm.) and n_D^{19} 1.4179. Petrov[10] reported b.p. 78.5–79° and n_D^{20} 1.4142 for 3,4-epoxy-3-methyl-1-butene prepared using *N*-bromoacetamide, then 80% potassium hydroxide.

β-(1-Aziridinyl)-α-methyl-α-vinylethanol (II). To a mixture of 10.0 g. (0.12 mole) of 3,4-epoxy-3-methyl-1-butene in 5 ml. of water was added dropwise with stirring 10.2 g. (0.24 mole) of ethylenimine dissolved in 5 ml. of water. The temperature was kept at 15–20° during the addition of the ethylenimine and for 3 hr. after the addition was complete. The reaction was left at room temperature for 16 hr. then evaporated to dryness *in vacuo*. The residue was distilled to give 10.6 g. (70%) of II b.p. 40–50° (0.1 mm.), n_D^{27} 1.4672; $\lambda_{max(\mu)}^{film}$ 2.95 (OH), 3.55 (aziridine CH), 6.07 (C=C). The vapor phase chromatogram[11] showed no detectable impurities.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.1; H, 10.3; N, 11.0. Found: C, 66.0; H, 10.5; N, 11.2.

By the same procedure *β-(1-aziridinyl)-α-ethylethanol* (III) was prepared from 10.0 g. of 1,2-epoxybutane[12] and ethylenimine; yield 8.0 g. (50%), b.p. 32–36° (0.1 mm.), n_D^{22} 1.4499; $\lambda_{max(\mu)}^{film}$ 2.97 (OH), 3.55 (aziridine CH). The product was 98% pure according to vapor phase chromatography.[11]

Anal. Calcd. for $C_6H_{13}NO$: C, 62.6; H, 11.4; N, 12.2. Found: C, 62.4; H, 11.4; N, 12.0.

β-(1-Aziridinyl)-α,β-dimethylethanol (IV). A mixture of 10.0 g. (0.14 mole) of 2,3-epoxybutane,[12] 12.0 g. (0.28 mole) of ethylenimine and 5 ml. of water was prepared as described in the preparation of β-(1-aziridinyl)-α-methyl-α-vinylethanol (II), then left for 72 hr. at room temperature. Distillation of the reaction mixture as described for II gave 7.15 g. (45%) of product (IV), b.p. 54–58° (3 mm.), n_D^{22} 1.4515; $\lambda_{max(\mu)}^{film}$ 2.97 (OH), 3.35–3.50 (aziridine CH). The vapor phase chromatogram showed that the distillate was 93% pure.

Anal. Calcd. for $C_6H_{13}NO$: C, 62.6; H, 11.4; N, 12.2. Found: C, 62.2; H, 11.6; N, 12.2.

A reaction time of 16 hr. gave only 5–10% yield.

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(8) LAC column, 70°.

(9) R. Pummerer and W. Reindel, *Ber.*, **66**, 335 (1933).

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(11) D C-710 column, 170°.

(12) Farchan Research Laboratories, 28915 Anderson Road, Wickliffe, Ohio.

3α-Hydroxy-19-nor-5α-androstan-17-one and 19-Nor-5α-androstane-3α-17β-diol[1,2]

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These compounds were prepared for the purpose of identifying metabolites of 19-nortestosterone.[3,4] 3β-Hydroxy-19-nor-5α-androstan-17-one was converted to the 3β-*p*-toluenesulfonate. The tosylate was treated with potassium acetate in dimethylformamide and the resulting 3α-acetoxy-19-nor-5α-androstan-17-one hydrolyzed in methanolic sodium hydroxide to 3α-hydroxy-19-nor-5α-androstan-17-one. Reduction of 3α-hydroxy-19-nor-5α-androstan-17-one with sodium borohydride yielded 19-nor-5α-androstane-3α,17β-diol.

(1) This work was supported in part by a grant from U.S.P.H.S. No. A-2672.

(2) The C-10 hydrogen in all compounds reported here has the β-configuration.

(3) D. Kupfer and E. Forchielli, *Federation Proc.*, **19**, 1968 (1960).

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EXPERIMENTAL[5]

3β-Hydroxy-19-nor-5α-androstane-17-one-p-toluenesulfonate (I). A 17-mg. sample of 3β-hydroxy-19-nor-5α-androstan-17-one (m.p. 177–179°)[6] was dissolved in 2.0 ml. dry pyridine containing 500 mg. of freshly recrystallized *p*-toluenesulfonyl chloride.[7] The solution was allowed to stand at room temperature for 24 hr. About 15 ml. of ice water was added and the resulting suspension extracted with cold chloroform. The chloroform phase was washed with cold 0.2*N* hydrochloric acid, cold 5% aqueous sodium bicarbonate and cold water till neutral, dried over sodium sulfate, and evaporated under reduced pressure to dryness. A 28.2-mg. sample of solid resulted (I); λ_{max}^{KBr} 5.78 (cyclopentyl C=O), 6.25 (phenyl C=C) 7.4, 8.5, and 14.95 μ; no hydroxyl absorption was present. A similar spectrum was obtained with the tosylate of epiandrosterone.

3α-Hydroxy-19-nor-5α-androstan-17-one (II) *from* (I). The crude tosylate (I) was dissolved in 4.0 ml. of dimethylformamide containing 180 mg. of potassium acetate in 0.5 ml. of water. The resulting solution was refluxed for 3 hr., allowed to stand overnight, and refluxed for an additional hour. Twenty milliliters of water was added to the precooled solution and the resulting suspension extracted with ether. The ether phase was washed with water, dried over sodium sulfate, and evaporated to dryness under reduced pressure. The resulting brown oil was extracted with petroleum ether (b.p. 30–60°) and the extract evaporated to dryness. A light yellow oil resulted (14.2 mg.); λ_{max}^{film} 5.75 (cyclopentyl ketone), 6.05 (C=C), 8.05 μ (acetate) and no hydroxyl present. The complex band at 8.05 μ similar to that of androsterone acetate indicated the presence of an axial acetate (3α,5α).[8] The crude oil was dissolved in 4.0 ml. methanol containing 55 mg. of potassium carbonate dissolved in 1.0 ml. of water and the mixture refluxed for 2 hr. Water was added to form a suspension which was extracted with about 100 ml. of ether, the ether phase was washed with water, dried over sodium sulfate, and evaporated to dryness under reduced pressure. The colorless oil obtained (8.5 mg.) was chromatographed on a silica gel column and eluted with benzene and benzene–ethyl acetate mixtures. The 2.7-mg. sample of white amorphous material which was eluted with benzene gave no significant ultraviolet absorption in the region of 220–360 mμ; λ_{max}^{KBr} 5.75 (cyclopentyl ketone), 6μ (isolated double bond), and no hydroxyl or acetate absorptions. Based on the infrared spectra and on reactions carried out under similar conditions with epiandrosterone[9] and allopregnane-3α-ol,11,20-dione[7] which yielded the corresponding Δ^2-elimination products, the compound is tentatively assigned the structure of Δ^2-19-norandrostan-17-one (m.p. 115–121°). Elution with benzene–ethyl acetate 9:1 and 6:1 resulted in 3.7 mg. of white amorphous material which upon crystallization from acetone-hexane yielded (II) colorless needles with the double melt 148°, 164.5–167°; $[\alpha]_D^{21.7}$ +110, (*c*, 0.765 in chloroform); λ_{max}^{KBr} 2.75 (OH), 5.75 (cyclopentyl C=O), 9.0, 9.35, 9.49, 9.65, 9.81, 10 μ (axial OH).[8]

19-Nor-5α-androstane-3α,17β-diol (III) *from* (II). A 2.1-mg. sample of II was dissolved in 1.0 ml. of methanol containing 15 mg. of sodium borohydride. The solution was stirred overnight, water was added, and the resulting suspension extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated to dryness. Chromatography on silica gel yielded 1.3 mg. of white amorphous material (III). Crystallization from acetone-hexane produced colorless needles, m.p. 191–193°; $[\alpha]_D^{21.1}$ + 23.7 (*c*, 0.34 in chloroform); λ_{max}^{KBr} 2.90 (bonded OH), and 9.15, 9.40, 9.55, 9.90, 10.00 μ (axial OH).[8] Oxidation of the diol with chromic acid in acetic acid produced a dione (λ_{max}^{KBr} 5.80, 5.87 μ) identical to an oxidation product of 19-nor-5α-androstane-3β,17β diol and to an authentic sample of 5α-19-norandrostane-3,17-dione.[10,11]

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(5) All melting points are uncorrected.
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(11) This compound was kindly supplied by Dr. Mika Hayano.

11-Oxygenated 17α-Acetoxy-9α-fluoro-6α-methyl-1,4-pregnadiene-3,20-diones

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Acylation of 9α-fluoro-11β,17α-dihydroxy-6α-methyl-1,4-pregnadiene-3,20-dione (I)[1,2] with acetic anhydride–*p*-toluenesulfonic acid[3] afforded 17α-acetoxy-9α-fluoro-11β-hydroxy-6α-methyl-1,4-pregnadiene-3,20-dione (II) in 45% yield. The 11-keto analog III was obtained by the chromic acid oxidation of II.

Endocrine assays of these compounds are summarized in Table I.

TABLE I

CORTICOID AND PROGESTATIONAL ASSAYS OF COMPOUNDS I, II, AND III

Compound	Anti-Inflammatory Activity (X Hydrocortisone) Rats	Glycogen Deposition (X Hydrocortisone)	Progestational (X Progesterone)
I	131[4]	26[4]	60
II	170[5]	7[5]	60–80[5]
III	40		

Compound II is the only steroid described as effectively inhibiting both the C-3-H mammary

(1) J. A. Hogg, 6th National Medicinal Chemistry Symposium, ACS, Madison, Wis., June 23, 1958.
(2) The registered trademark of the Upjohn Company, Kalamazoo, Mich., for 9α-fluoro-11β,17α-dihydroxy-6α-methyl-1,4-pregnadiene-3,20-dione is Oxylone.
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