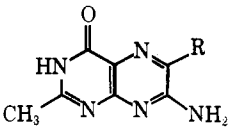
TABLE I

6-SUBSTITUTED 7-AMINO-4-HYDROXY-2-METHYLPTERIDINES



| Compd | R | Formula[a] | Yield, % | Mp, °C | Appearance |
|---|---|---|---|---|---|
| II | $COOC_2H_5$ | $C_{10}H_{11}N_5O_3$ | 45 | >300 | Pale brown needles |
| III | $CONH_2$ | $C_8H_8N_6O_2$ | 90 | >300 | Dark yellow prisms |
| IV | $C_6H_5$ | $C_{13}H_{11}N_5O$ | 30 | >300 | Dark yellow prisms |
| V | CN | $C_8H_6N_6O$ | 64 | >300 | Dark yellow powder |

[a] All compds were analyzed for C, H, N.

search for new chemotherapeutics led to the synthesis of some pteridine-6-carboxylic acids and related compounds, which possess structures somewhat similar to that of nalidixic acid. None of the products obtained exhibited activity against *Escherichia coli*, *Staphylococcus aureus* 209 P, and *Trichophyton asteroides* (Juntendo strain) at 100 μg/ml.

### Experimental Section[2]

**Ethyl 7-Amino-4-hydroxy-2-methylpteridine-6-carboxylate (II).**—4-Amino-6-hydroxy-2-methyl-5-nitrosopyrimidine[3] (I) (0.77 g, 0.005 mole) was dissolved in hot DMF (15 ml). To this soln, $NCCH_2CO_2Et$ (0.67 g, 0.0055 mole) and NaOMe (0.54 g, 0.01 mole) were added and refluxed for 2 hr. After the reaction mixt was concd, the pptd product was filtered off, dissolved in hot $H_2O$, and acidified with AcOH to give pale brown powder, which was collected by filtration and recrystd from DMF. Compds III, IV, and V were prepared by this procedure.

**2,6,8-Trimethyl-4,5,7(3*H*,6*H*,8*H*)pyrimido[5,4-*g*]pteridinetrione (VI).**—A mixt of 4-amino-6-hydroxy-2-methyl-5-nitrosopyrimidine[3] (I) (1.54 g, 0.01 mole) and 4-amino-1,3-dimethyluracil (1.55 g, 0.01 mole) in AcOH (15 ml) was refluxed for 3 hr. After cooling, the pptd crystals were collected by filtration and recrystd from AcOH to yield 1.2 g (45%) of red crystals, mp >320°. *Anal.* ($C_{11}H_{10}N_6O_3 \cdot H_2O$) C, H, N.

**Ethyl 7-Acetamino-4-hydroxy-2-[2-(5-nitro-2-furyl)vinyl]-pteridine-6-carboxylate (VIII).**—A mixt of 0.5 g (0.002 mole) of II and 0.3 g (0.002 mole) of 5-nitrofurfural in 4 ml of AcOH–$Ac_2O$ (1:1) was heated under reflux for 3 hr. After cooling, the product was filtered off, dried, and recrystd from DMF to give 0.6 g (75%) of dark yellow powder, mp 275° dec. *Anal.* ($C_{17}H_{14}N_6O_7$) C, H, N.

**7-Acetamino-4-hydroxy-2-[2-(5-nitro-2-furyl)vinyl]pteridine-6-carboxylic Acid (VIII).**—To a mixt of 20 ml of AcOH and 1.8 ml of concd HCl was added 0.6 g (0.0015 mole) of VII, and the whole was heated for 2 hr at 130°. After concn of the reaction mixt, the pptd crystals were collected by filtration and dried. Recryst from DMF gave 0.4 g (69%) of dark yellow powder, mp >320°. *Anal.* ($C_{15}H_{10}N_6O_7$) C, H, N.

(2) Where analyses are indicated only by the symbols of the elements, anal. values are within 0.4% of the theor values.

(3) P. D. Landauer and H. N. Pydon, *J. Chem. Soc.*, 3721 (1953).

## *A*-Norandrogens

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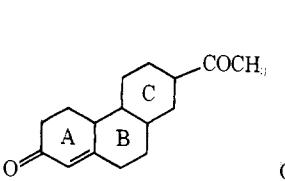
Dorfman and Stevens[1] have reported that 2-acetyl-7-oxo-1,2,3,4,4α,4β,5,6,7,9,10,10α-dodecahydrophenanthrene (**1**) possesses both androgenic activity in the chick and antiandrogenic properties in the rat. Similarly 2-(1-ethynyl-1-hydroxyethyl)-7-oxo-1,2,3,4,4α,4β,5,6,7,9,10,10α-dodecahydrophenanthrene (**2**) has been reported by Boris[2] to possess antiandrogenic as well as progestational activity. The compds when compared to steroid structure lack the D ring and the angular Me groups. Rings A, B, and C must bind strongly to the receptor site to elicit the reported responses. Our work on *A*-norsteroids was initiated to investigate if rings B, C, and D would be equally strong in their binding ability. The general procedure is outlined in the Experimental Section. All compds (Table I) were submitted to a preliminary screen for androgenic, anabolic, and antiandrogenic activity.[3] None of the compds exhibited significant activity.



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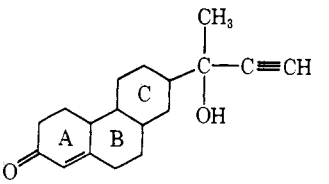
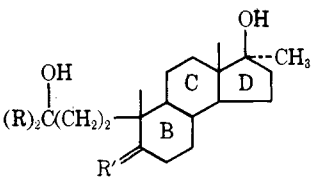


2

TABLE I

*A*-NORANDROGENS



| Compd[a] | R | R′ | Recrystn solvent | Mp, °C[b] | Formula[c] |
|---|---|---|---|---|---|
| 1 | $CH_3$ | $CH_3$, OH | MeOH | 214–215 | $C_{22}H_{40}O_3$ |
| 2 | $C_2H_5$ | $C_2H_5$, OH | MeOH | 204–205 | $C_{25}H_{46}O_3$ |
| 3 | $C_6H_5$ | 0 | Hexane | 100–102 | $C_{31}H_{40}O_3$ |
| 4 | *p*-Anisyl | 0 | Hexane | 85–88 | $C_{33}H_{44}O_5$ |

[a] Structure confirmed by spectral data. [b] Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. [c] Elemental anal. were within ±0.4% of the theor values.

### Experimental Section

**General Procedure for Grignard Reactions. 3,3,5 and 17α-Tetramethyl-3,5-seco-4-norandrosta-3,5- and -17β-triol (1).**—Methyl 17α-methyl-3,5-seco-4-norandrostan-17β-ol-5-on-3-oate (1.0 g) was dissolved in 50 ml of PhH and added slowly to a stirred soln of 30 ml of MeMgBr in $Et_2O$. The mixt was refluxed for 16 hr and excess Grignard reagent decompd with ice water and satd aq $NH_4OAC$. The org layer was washed ($H_2O$) until neutral, dried ($Na_2SO_4$), and evapd to give a residue. Analytically pure sample of **1** was recrystd from MeOH, mp 214–215°.

**Acknowledgment.**—The author wishes to express his appreciation to Dr. I. Scheer for his understanding and encouragement and to Mr. G. Allen for the pharmacological evaluations.

(1) R. I. Dorfman and D. Stevens, *Endocrinology*, **67**, 394 (1960).

(2) A. Boris, *ibid.*, **76**, 1062 (1965).

(3) L. G. Herschberger, E. G. Shipley, and R. K. Meyer, *Proc. Soc. Exp. Biol. Med.*, **83**, 175 (1953).