diazo-5-methylpyrazole-3-carboxamide and Me_2NH in a similar fashion. *Anal.* ($C_7H_{12}N_6O$) C, H, N.

Ethyl 3-(4-Carbamoylpyrazole-3-yl)-2-triazenoacetate (II).—To a mixt of 40 g of finely powdered glycine·HCl Et ester in 600 ml of EtOAc was added 30 g of Et_3N. The resulting mixt was stirred at room temp for 1 hr. To this was added 20 g of powdered 3-diazopyrazole-4-carboxamide[3] and the mixt was stirred for 24 hr. The solid was collected by filtration and extd repeatedly with hot 50% aq MeOH. The insol solid, which melted at 220–222° dec and possessed $\lambda_{max}^{pH\ 11}$ at 402 nm, has not yet been identified. The filtrate was concd *in vacuo* to yield 9 g of analytically pure II, mp 145°. *Anal.* ($C_5H_{12}N_6O_3 \cdot H_2O$) C, H, N, H_2O.

1-[(4-Carbamoylpyrazol-3-yl)azo]DL-proline (III).—To a mixt of 20 g of finely powdered 3-diazopyrazole-4-carboxamide[3] in 500 ml of MeOH was added 40 g of finely powdered DL-proline. The mixt was stirred at 25° for 18 hr and the solid collected by filtration. It was recrystd from 50% aq MeOH to give 5 g of III, mp 188–189°. *Anal.* ($C_9H_{12}N_6O_3$) C, H, N.

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Steroidal Heterocycles. 14.[1] 1,8a-Epoxy-1,4,4a,5,6,7,8,8a-octahydro-2-hydroxynaphthalene-3-carbonitrile and Related Compounds

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4α,5-Epoxy-3,17β-dihydroxy-5α-androst-2-ene 2-carbonitrile (**9**) and related steroids block the ACTH-induced catabolic and thymolytic responses in castrate male rats.[1] Therefore, it seemed of interest to determine whether related bicyclic compds resembling rings A/B of these steroids would exhibit similar activity. Using known procedures[2-4] indicated in the flow sheet, 2-methylcyclohexanone (**1**) was converted in a series of steps into 1,8a-epoxy-1,4,4a,5,6,7,8,8a-octahydro-4a-methylnaphtho[2,3-*d*]isoxazole (**7**) which was rearranged to **8** with base.

Biological Testing.—Compd **8** showed none of the ACTH-induced catabolic blocking of the corresponding steroid **9** in castrated rats. It did exhibit slight bacteriostatic and fungistatic activities.

Experimental Section

All melting points were taken on a Fisher-Johns melting point apparatus, uncor. Uv spectra were detd in 95% EtOH (Cary 15) and ir in KBr disks (Perkin-Elmer 21). Nmr spectra were measured with (Me_4Si) in $CDCl_3$ (Varian A60). Where analyses are indicated only by symbols of the elements, anal. results obtained for those elements were within ±0.4% of the theor values.

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(1) H. C. Neumann, G. O. Potts, W. F. Ryan, and F. W. Stonner, *J. Med. Chem.*, **13**, 948 (1970).

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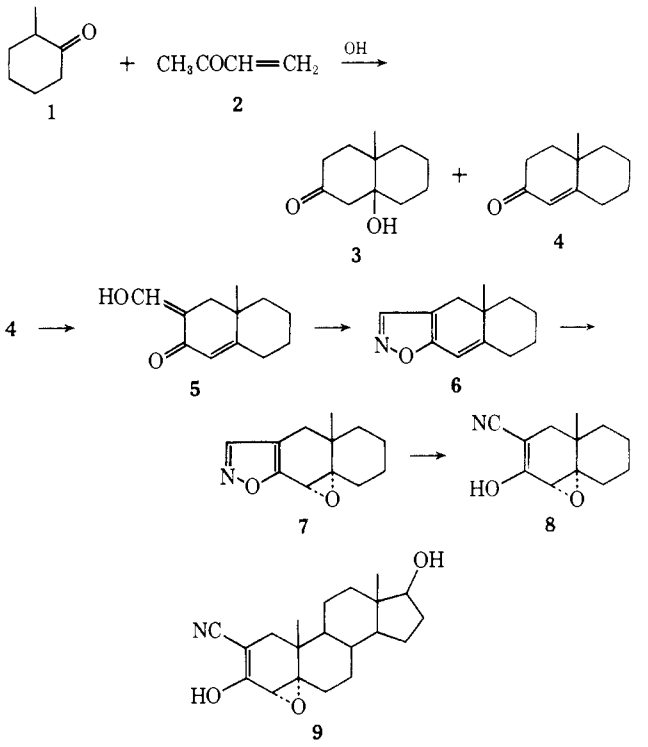

1,8a-Epoxy-1,4,4a,5,6,7,8,8a-octahydro-4a-methylnaphtho[2,3-*d*]isoxazole (7).—The distd hydroxymethylene compd **5**[3] gave an isoxazole **6** with H_2NOH,[3] obtd as an amber resin. Crude resin **6** (no attempt was made to purify **6**) (17.5 g) was dissolved in CH_2Cl_2 (300 ml) and added to H_2O_2 (6 ml; 1.3 g/ml) and maleic anhydride (20 g) in CH_2Cl_2 (100 ml) at 0°.[4] The soln was swirled vigorously, and C_5H_5N (5 drops) was added. The soln became turbid immediately as maleic acid pptd and was kept in a refrigerator overnight. Satd Na_2SO_3 soln was added dropwise with stirring until starch–iodide paper no longer darkened. The soln was washed with $NaHCO_3$ soln, dried ($MgSO_4$), filtered, and concd on a steam bath. Faint yellow, cryst material was obtained (8.89 g; 46.8% yield); the rest was dark amber resin. The product was crystd (EtOAc): mp 85–86°; λ_{max} 237 mμ (6850). *Anal.* ($C_{12}H_{15}NO_2$) C, H, N.

1,8a-Epoxy-1,4,4a,5,6,7,8,8a-octahydro-2-hydroxy-8a-methylnaphthalene-3-carbonitrile (8).—Isoxazole **7** (19.5 g) was dissolved in THF (200 ml), stirred, and cooled in an ice bath. NaOMe (10.8 g) was added and soon a thick ppt of the Na salt of **8** formed. After 2 hr of stirring, Et_2O (100 ml) was added, and the salt was filtered and rinsed with Et_2O. After most of the Et_2O adhering to the salt had dissipated, it was dissolved in H_2O (200 ml), Na_2HPO_4 (10 g) was added, and the soln was acidified with dil HCl. The oily ppt was extd with Et_2O, dried ($MgSO_4$), and concd on a steam bath to afford 18.5 g (85%) of granular crystals, mp 98–100°. They were recrystd (EtOAc): mp 100–102°; λ_{max} 252 mμ (9400), ir 4.54, 5.81 (weak, medium), 6.16 μ. Nmr also indicated a mixt of keto–enol tautomers.[1] *Anal.* ($C_{12}H_{15}NO_2$) C, H, N.

Synthesis of 2-Methylpteridine Derivatives

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We have previously reported on pyrido[2,3-*d*]pyrimidine derivatives, which are potential pteridine antagonists as well as azalogs of nalidixic acid.[1] A continuing

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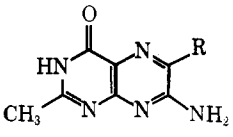
TABLE I

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.

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A-Norandrogens

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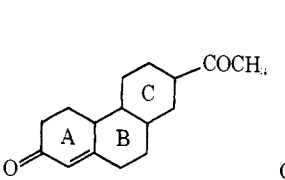
Dorfman and Stevens[1] have reported that 2-acetyl-7-oxo-1,2,3,4,4α,4β,5,6,7,9,10,10α-dodecahydrophenanthrene (**1**) possesses both androgenic activity in the chick and antiandrogenic properties in the rat. Similarly 2-(1-ethynyl-1-hydroxyethyl)-7-oxo-1,2,3,4,4α,4β,5,6,7,9,10,10α-dodecahydrophenanthrene (**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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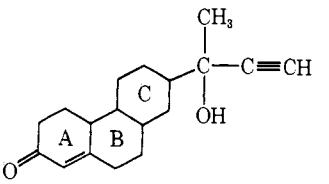

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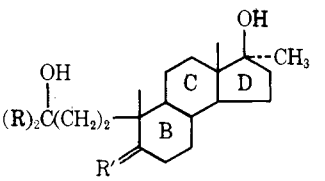
TABLE I

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.

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

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