

matic proton in the reduction product (II) appears at 6.30 δ aflatoxin B has structure I.

The substance with yellow-green fluorescence, C₁₇H₁₂O₇, mol. wt. 328 (mass. spec.), m.p. 244–246° dec., $[\alpha]_D^{CHCl_3}$ -556°; λ_{max}^{EtOH} 243, 257, 264, 362 m μ (ϵ 11,500; 9,900; 10,000; 16,100); $\mu_{max}^{CHCl_3}$ 1760, 1695, 1630, 1595 cm.⁻¹ is identical with aflatoxin G.³ Its n.m.r. spectrum exhibits an A₂X₂ pattern at 4.47 (triplet, $J = 6$ c.p.s., 2H) and 3.48 δ (triplet, $J = 6$ c.p.s., 2H). The chemical shifts and multiplicities for all other protons are identical with those of aflatoxin B(I) and we conclude that aflatoxin G has structure IV.

Acute toxicities were determined by biological assay in day-old White Pekin ducklings. Groups of ten animals weighing 51 ± 4 g. received various dose levels of the appropriate compound dissolved in propylene glycol, each animal receiving 0.1 ml. by stomach tube. Mortality and body weights were recorded 48 hr. after administration. Under these conditions the LD₅₀ for aflatoxin B (I) was calculated as 28.2 μ g. with 95% confidence limits of 24.7 and 32.2 μ g. The LD₅₀ for aflatoxin G (IV) was estimated to be 90 μ g. Administration of 50 μ g. of the reduction product (II) resulted in no mortality compared to 100% mortality with the same dose of the parent compound (I).

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SYNTHESIS OF 19-NOR STEROIDS. II.
d,l-17 α -CHLOROETHYNYL-19-NOR-4,10(9),8(14)-
ANDROSTADIENE-17 β -OL-3-ONE¹

Sir:

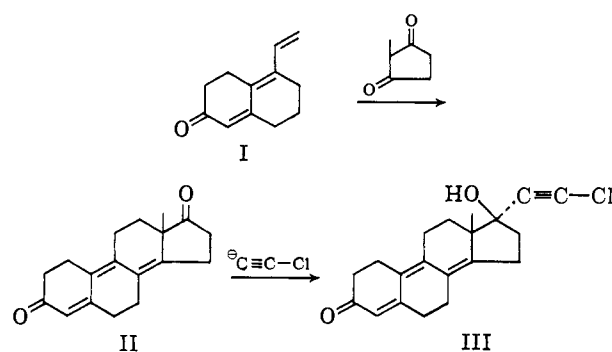
It was shown previously² that introduction of a C-9, 10 double bond markedly enhances the gonadotrophin inhibiting activity of 17 α -chloroethynyl-19-nor-4-androstene-17 β -ol-3-one. It was, therefore, of interest to determine whether an additional double bond at C-8,14 would further potentiate activity.

We wish to report the preparation of *d,l*-17 α -chloroethynyl-19-nor-4,10(9),8(14)-androstadiene-17 β -ol-3-

(1) Part I: T. B. Windholz, J. H. Fried and A. A. Patchett, *J. Org. Chem.*, **28**, 1092 (1963).

(2) J. H. Fried, T. S. Bry, A. E. Oberster, R. E. Beyler, T. B. Windholz, J. Hannah, L. H. Sarett and S. L. Steelman, *J. Am. Chem. Soc.*, **83**, 4863 (1961); cf. M. Perelman, E. Farkas, E. J. Fornefeld, R. J. Kraay and R. T. Rapala, *ibid.*, **82**, 2402 (1960).

one (III) and its precursor, *d,l*-19-nor-4,10(9),8(14)-androstatriene-3,17-dione (II) by a relatively short synthesis.



Reaction of (I)³ with 2-methylcyclopentane-1,3-dione⁴ in the presence of diethylamine afforded II, m.p. 131–132°; ultraviolet λ_{max}^{MeOH} 350 m μ , ϵ 24,200 (*Anal.* Found: C, 80.90; H, 7.60). It is interesting to note that both Michael condensation and cyclodehydration occurred in the basic condensing medium in ca. 17% yield, in view of earlier reports^{5,6} that in analogous systems acid is required to accomplish the dehydration reaction.

Selective chloroethynylation of II at C-17 was achieved using sodium chloroacetylide in liquid ammonia⁷ to yield III, m.p. 159–160°; ultraviolet λ_{max}^{MeOH} 358 m μ , ϵ 19,900 (*Anal.* Found: C, 72.97; H, 6.45).

Preliminary test results⁸ with racemic III showed oral gonadotrophin inhibition⁹ (parabiotic rats) and oral progestational activity¹⁰ of 1.5–2.0 \times 17 α -ethynyl-19-nor-4-androstene-17 β -ol-3-one.¹¹

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(3) N. N. Gaidamovich and I. V. Torgov, *Izv. Akad. Nauk. SSSR, Old. Khim. Nauk*, 1162 (1961), and references cited therein. These authors have prepared the D-homo analog of (II) using 8-oxo-1-vinyl-2,3,4,8,7,8-hexahydronaphthalene (I) and 2-methylcyclohexane-1,3-dione.

(4) J. J. Panouse and Ch. Sannié, *Bull. soc. chim. France*, 1036 (1955).

(5) A. Eschenmoser, J. Schreiber and S. A. Julia, *Helv. Chim. Acta*, **36**, 482 (1953).

(6) J. J. Panouse and Ch. Sannié, *Bull. soc. chim. France*, 1429 (1956).

(7) H. G. Viehe, *Chem. Ber.*, **92**, 1270 (1959).

(8) We wish to thank Dr. S. L. Steelman of the Merck Institute for Therapeutic Research for performing these tests.

(9) J. A. Epstein, H. S. Kupperman and A. Cutler, *Ann. N. Y. Acad. Sci.*, **71**, 560 (1958).

(10) M. K. McPhail, *J. Physiol.*, **83**, 145 (1934).

(11) In this assay 17 α -chloroethynyl-19-nor-4,10(9)-androstadiene-17 β -ol-3-one has an activity of 6–8 \times 17 α -ethynyl-19-nor-4-androstene-17 β -ol-3-one (ref. 2).