C, 29.5; H, 3.5. The ultraviolet absorption spectra of III at *p*H 1 showed $\lambda_{max.}$ 252 mμ, E 5,800, at *p*H 11 $\lambda_{max.}$ 270 mμ, E 8,000.

A complete description of the experimental procedure involved in the stepwise synthesis of III will appear in a forthcoming publication involving other related work. 4-Hydroxy-6-aminopyrazolo-[3,4-*d*]pyrimidine (III) is currently being tested in several laboratories for anti-tumor action. Dr. L. W. Law and Dr. S. E. Reaume of the Leukemia Studies Section of the National Cancer Institute in preliminary studies have found III to show activity of varying extent against three lymphocytic neoplasms of the mouse, L-1210, L-5178, and L-4946. These results when completed will be reported elsewhere.

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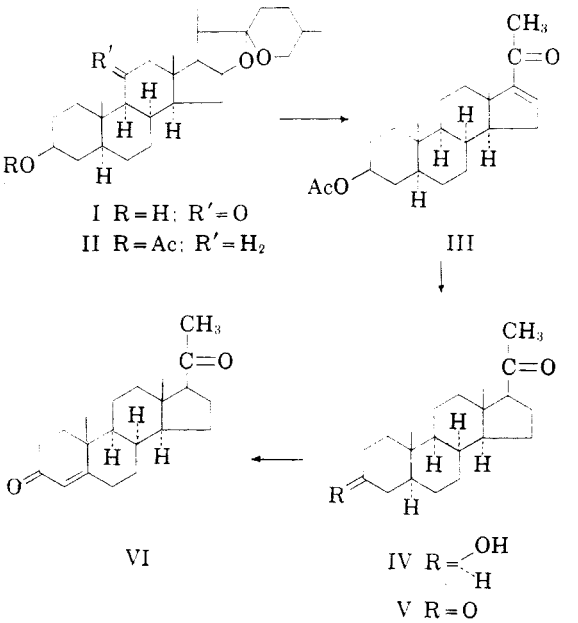
8-Isoprogesterone

Sir:

Much of the recent emphasis in the steroid field has been concerned with the synthesis of hormone analogs which could fulfill one of the following functions: (a) increased hormonal activity, (b) hormone antagonism or (c) separation of certain hormonal from other physiological effects (*e.g.*, nonandrogenic anabolic agents). Our own efforts in this field have centered on the preparation of certain isomers which differ from the natural hormones only in the stereochemistry of a relatively inaccessible center and on determining the consequences of such a subtle change upon biological activity. The stereoselective preparation of certain 11-oxygenated sapogenins[1] differing only in the orientations of C-8 and/or C-14 has led us to examine some derived steroids and the synthesis of 8-isoprogesterone (VI) is recorded herewith. This isomer of progesterone was considered to be a particularly appropriate test case since progestational activity is known[2] to be extremely specific and dependent upon precise structural and stereochemical features.

Modified Wolff-Kishner reduction[3] of 22a,25a,-5α,8α-spirostan-3β-ol-11-one (I)[1] followed by acetylation led to 22a,25a,5α,8α-spirostan-3β-ol acetate (8-isotigogenin acetate) (II), m.p. 186–189°, $[\alpha]_D$ −10° (all rotations in chloroform); *Anal.* Calc'd for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.73; H, 10.33. Application of the standard side chain degradation produced Δ^{16}-8α-allopregnen-3β-ol-20-one acetate (III) (m.p. 178–180°, $[\alpha]_D$ +118°, λ_{max}^{EtOH} 240 mμ, log ε 4.00; *Anal.* Calc'd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 76.94; H, 9.40) which was hydrogenated (palladized charcoal catalyst in ethyl acetate solution) and saponified[4] to yield 8α-allopregnan-3β-ol-20-one (IV) (m.p. 184–187°, $[\alpha]_D$ +149°; *Anal.* Calc'd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.14; H, 10.76). Chromium trioxide oxidation of IV furnished 8α-allopregnane-3,20-dione (V) (m.p. 173–176°, $[\alpha]_D$ +144°; *Anal.* Calc'd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.90; H, 10.31), while the subsequent introduction of the 4,5-double bond was patterned after that employed for the synthesis of 11α-hydroxyprogesterone.[5]



The resulting 8-isoprogesterone (VI) (m.p. 144–147°, $[\alpha]_D$ +130°, $\lambda_{max}^{CHCl_3}$ 5.86, 5.98, and 6.12 μ, λ_{max}^{EtOH} 241 mμ, log ε 4.18; *Anal.* Calc'd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 79.95; H, 9.67) was subjected to biological testing in rabbits using suitable controls treated with progesterone. In the standard Clauberg test,[6] 8-isoprogesterone (VI) by subcutaneous injection in a total of 12 animals exhibited between one-half to one-fourth the progestational activity, while local injection (into the uterine lumen) by the McGinty technique[7] in 12 animals indicated the same order of activity

(1) Djerassi and Thomas, *Chemistry & Industry*, 1228 (1954). Djerassi, Frick, Rosenkranz and Sondheimer, *J. Am. Chem. Soc.*, **75**, 3496 (1953).

(2) *Cf.* Djerassi, Miramontes, and Rosenkranz, *J. Am. Chem. Soc.*, **75**, 4440 (1953); Gunthard, Beriger, Engel, and Heusser, *Helv. Chim. Acta*, **35**, 2437 (1952); Ehrenstein, *Chem. Revs.*, **42**, 457 (1948).

(3) Barton, Ives, and Thomas, *J. Chem. Soc.*, 2056 (1955).

(4) That no isomerization had occurred during the alkali treatment was established by re-acetylation to the original acetate.

(5) Mancera, Romo, Sondheimer, Rosenkranz, and Djerassi, *J. Org. Chem.*, **17**, 1066 (1952).

(6) *Cf.* Emmens, *Hormone Assay*, Academic Press, New York, 1950.

(7) McGinty, Anderson, and McCullough, *Endocrinology*, **24**, 829 (1939).

as the parent hormone. It can be concluded, therefore, that isomerization at C-8 of progesterone does not result in any marked diminuition of hormonal activity.

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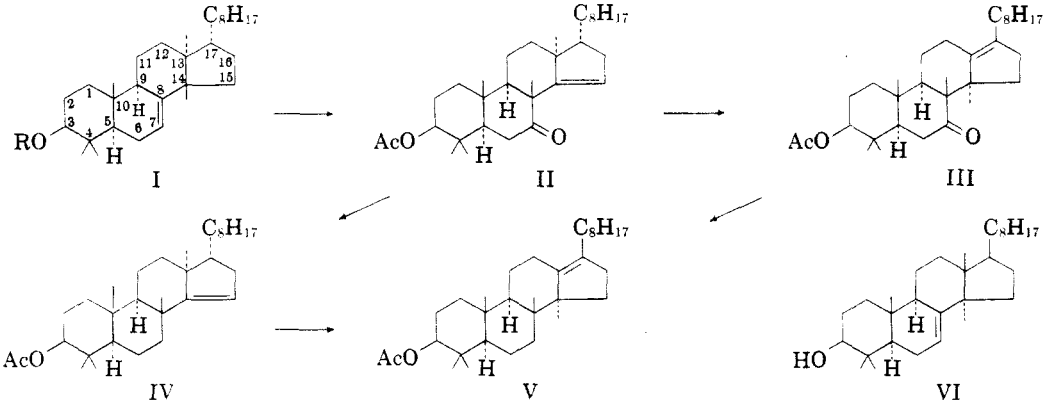
The Constitution of Butyrospermol

Sir:

A recent Communication[1] described the conversion of butyrospermol into euphol. Osmic acid converts dihydrobutyrospermyl acetate into a triol which forms a diacetate [m.p. 181–182°, $[\alpha]_D$ −82° (*c*, 1.2).[2] Found: C, 74.9; H, 10.9. $C_{34}H_{58}O_5$ requires C, 74.7; H, 10.7] and this on heating at 100° gives eupha-7:9(11)-dienyl acetate [m.p. and mixture m.p. 111–112°, $[\alpha]_D$ −78° (*c*, 1.0), $\lambda_{max.}$ 2320, 2400 (log. ϵ = 4.24) and 2470 Å.]. The less reactive double bond in butyrospermol is therefore trisubstituted and not tetrasubstituted[3] and this alcohol is either a 9ξ-eupha-7:24-dien-3β-ol or an 8ξ-eupha-9(11):24-dien-3β-ol.[1,4] We now wish to describe experiments which identify butyrospermol as 9α-eupha-7:24-dien-3β-ol.

Oxidation of dihydrobutyrospermyl acetate (I, R = Ac) with chromic acid yields 7-oxo*apo*euph-14-enyl acetate (II) [m.p. 119–120°, $[\alpha]_D$ −85° (*c*, 1.0), ϵ_{2100} = 5,400; I.R. bands at 1735 (acetate) and 1710 cm.$^{-1}$ (six-ring ketone). Found: C, 79.2; H, 11.1. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8], which with mineral acid gives 7-oxo*iso*euph-13(17)-enyl acetate (III) [m.p. 112–113°, $[\alpha]_D$ −50° (*c*, 1.3), ϵ_{2100} = 6,700. Found: C, 79.6; H, 11.0. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8]. Wolff-Kishner reduction of III, and reacetylation, gives *iso*euph-13(17)-enyl acetate (V)[5] [m.p. and mixture m.p. 110°, $[\alpha]_D$ −9° (*c*, 2.0). Found: C, 81.7; H, 11.7. Calc'd for $C_{32}H_{54}O_2$: C, 81.6; H, 11.6]. Oxidation of III with selenium dioxide yields 7-oxo*iso*eupha-11:13(17)-dienyl acetate [m.p. 107–109°, $[\alpha]_D$ −45° (*c*, 0.2), $\lambda_{max.}$ 2470, 2550 (log. ϵ = 4.33) and 2640 Å. Found: C, 79.4; H, 10.45. $C_{32}H_{50}O_3$ requires C, 79.6; H, 10.4]. Wolff-Kishner reduction of 7-oxo*apo*euph-14-enyl acetate (II), and re-acetylation gives *apo*euph-14-enyl acetate (IV) [m.p. 114–115°, $[\alpha]_D$ −12° (*c*, 1.1), ϵ_{2100} = 5,300. Found: C, 81.5; H, 11.7. $C_{32}H_{54}O_2$ requires C, 81.6; H, 11.6] isomerized by a short treatment with dry hydrogen chloride at 0° to *iso*euph-13(17)-enyl acetate (V)[5] [m.p. and mixture m.p. 109–110°, $[\alpha]_D$ −10° (*c*, 0.4)]. These acid conditions have no effect upon euph-8-enyl acetate and simply convert dihydrobutyrospermyl acetate (I, R = Ac) into euph-8-enyl acetate.[1] Selenium dioxide converts 7-oxo*apo*euph-14-enyl acetate (II) into 7-oxo*apo*eupha-5:14-dienyl acetate [m.p. 103–104°, $[\alpha]_D$ −126° (*c*, 1.2), $\lambda_{max.}$ 2350 Å. (ϵ = 14,000). Found: C, 79.4; H, 10.4. $C_{32}H_{50}O_3$ requires C, 79.6; H, 10.4].



The oxidation of dihydrobutyrospermyl acetate to 7-oxo*apo*euph-14-enyl acetate (II) establishes that the double bond in the former is between C_7 and C_8. We understand that Professor E. R. H.

(1) D. S. Irvine, W. Lawrie, A. S. McNab, and F. S. Spring, *Chemistry & Industry*, 626 (1955).

(2) Specific rotations are for chloroform solutions at 15°.

(3) K. Seitz and O. Jeger, *Helv. Chim. Acta*, **32**, 1626 (1949); T. G. Halsall, *Chem. and Ind.*, 867 (1951).

(4) M. C. Dawson, T. G. Halsall, E. R. H. Jones, G. D. Meakins, and P. C. Phillips, *Chemistry & Industry*, 918 (1955); E. R. H. Jones and T. G. Halsall, *Fortschritte der Chemie organischer Naturstoffe*, Springer-Verlag, **XII**, 108 (1955).

(5) D. H. R. Barton, J. F. McGhie, M. K. Pradhan, and S. A. Knight, *J. Chem. Soc.*, 876 (1955).