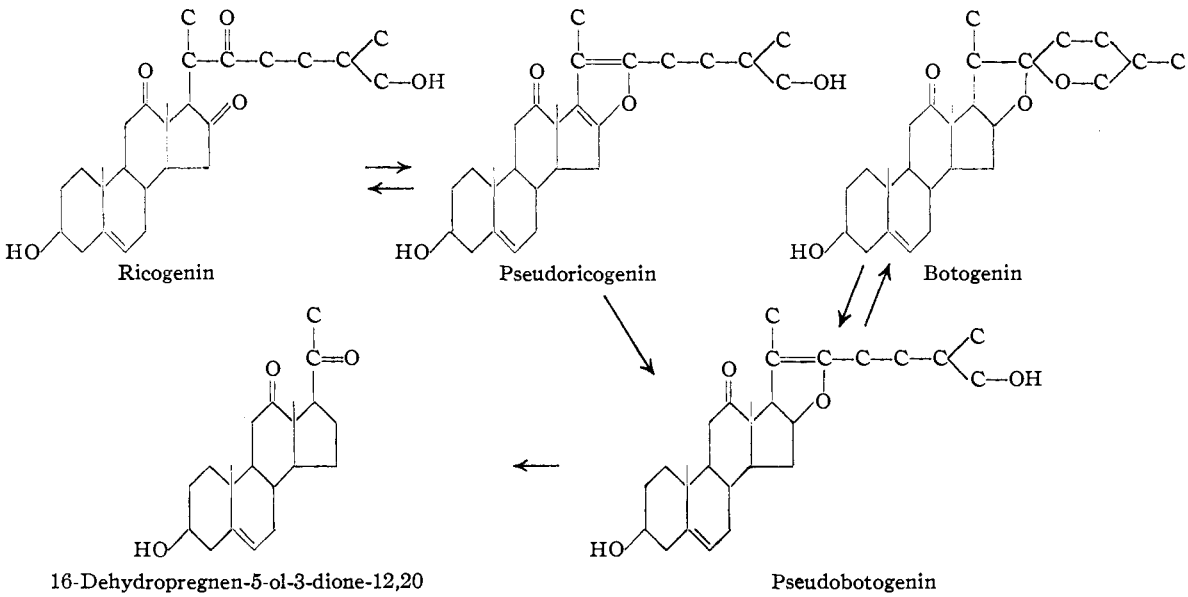
STEROIDAL SAPOGENINS, 173. 16-DEHYDROPREGNEN-5-OL-3-DIONE-12,20 FROM RICOGENIN, A NEW STEROIDAL SAPOGENIN

Sir:

In an extensive search for naturally occurring steroidal sapogenins having substituents in ring C which may be utilized for the synthesis of cortisone, the anti-arthritic hormone, a new saponide, riconin, m.p. 285–289° dec., was isolated from the mixture of glycosides occurring in *Dioscorea Macrostachya*.



Hydrolysis of riconin with alcoholic hydrochloric acid gave ricogenin, m.p. 225–227°. *Anal.* Calcd. for $C_{27}H_{40}O_5$: C, 72.9; H, 9.1. Found: C, 72.9; H, 9.1.

Ricogenin formed a diacetate, m.p. 195–197°, and contains three ketonic groups having the same side-chain structure as kryptogenin. *Anal.* Calcd. for $C_{31}H_{44}O_7$: C, 70.4; H, 8.4. Found: C, 70.2; H, 8.2.

Treatment of ricogenin with acetic anhydride at 195° for eight hours followed by hydrolysis gave pseudoricogenin, m.p. 220–222°. *Anal.* Calcd. for $C_{27}H_{38}O_4$: C, 76.0; H, 9.0. Found: C, 76.2; H, 9.0.

When heated with alcoholic hydrochloric acid for fifteen minutes, pseudoricogenin was converted into ricogenin, m.p. and mixed m.p. 225–227°. Catalytic reduction of the diacetate of pseudoricogenin, using palladium-on-barium sulfate as catalyst, saturated only the conjugated double bond in ring D, giving the diacetate of pseudobotogenin. This product upon alkaline hydrolysis followed by isomerization with alcoholic hydrochloric acid gave botogenin, m.p. and mixed m.p. 260–262°. *Anal.* Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.5; H, 9.4.

Acetylation of this product gave botogenin acetate, m.p. and mixed m.p. 246–248°. *Anal.* Calcd. for $C_{29}H_{42}O_5$: C, 74.0; H, 9.0. Found: C, 74.1; H, 9.3.

The pseudobotogenin diacetate produced by the catalytic reduction of the diacetate of pseudoricogenin was oxidized with chromic anhydride in acetic acid, followed by hydrolysis,[1] giving 16-dehydropregnen-5-ol-3-dione-12,20 acetate, m.p. and mixed m.p. with the product prepared from naturally occurring botogenin, 225–227°. *Anal.* Calcd. for $C_{23}H_{30}O_4$: C, 74.8; H, 8.2. Found: C, 74.6; H, 81.

(1) Marker, THIS JOURNAL, 71, 2660 (1949).

BOTANICA-MEX, S. A.
PLAZA DE SAN PABLO NO. 6 RUSSELL E. MARKER
TEXCOCO, MEXICO HOTEL GENEVE, MEXICO CITY

RECEIVED OCTOBER 4, 1949

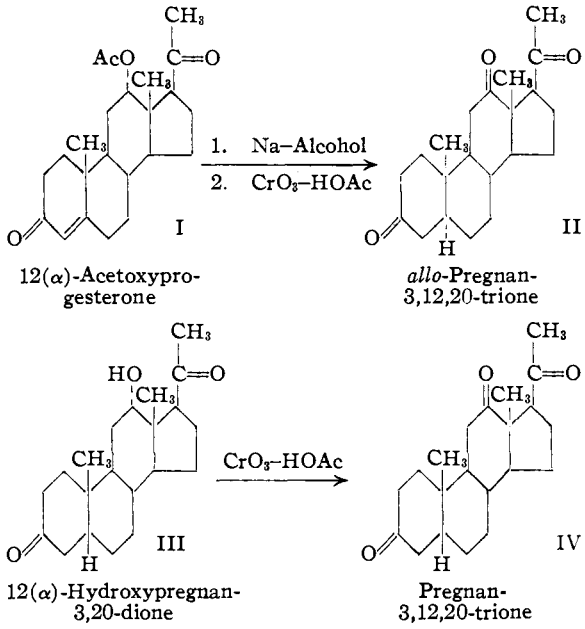
ALLO-PREGNAN-3,12,20-TRIONE

Sir:

The current interest in Kendall's substance E for rheumatoid arthritis has stimulated great interest in the search for starting materials for its synthesis. Recently, Marker reported the possibility of utilizing a steroidal sapogenin, botogenin, isolated from *Dioscorea Mexicana*.[1] Its degradation product was 5-pregnen-3(β)-ol-12,20-dione, characterized by conversion to *allo*-pregnan-3,12,-20-trione, m.p. 264°. The latter was identical with *allo*-pregnan-3,12,20-trione[2] from the degradation of hecogenin.

We have prepared an authentic sample of *allo*-pregnan-3,12,20-trione by an entirely different route and have found it completely different from the trione from hecogenin. Desoxycholic acid has been degraded to 12(α)-acetoxyprogesterone (I), m.p. 181°, $[\alpha]^{26}D$ +215°, $[\alpha]^{25}_{5461}$ +259° (chloroform), absorption maximum at 240mμ(log ε 4.14 in ethanol).[3] This compound (I) upon sodium–alcohol reduction followed by chromic acid oxidation furnished *allo*-pregnan-3,12,20-trione (II), m.p. 206–208°, $[\alpha]^{23}D$ +184°, $[\alpha]^{23}_{5461}$ +224° (chloroform), no maximum at 240mμ. *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.3; H, 9.2. Found: C, 76.0; H, 8.9. The reduction was also accomplished with hydrogen and Adams catalyst in acetic acid; subsequent hydrolysis and oxidation gave the same product (II). The course of these methods of reduction has been shown previously[4]

(1) Marker, THIS JOURNAL, 71, 2656 (1949).
(2) Marker, Wagner and co-workers, *ibid.*, 69, 2167 (1947).
(3) Shoppee and Reichstein, *Helv. Chim. Acta*, 24, 351 (1941).
(4) Marker and Wittle, THIS JOURNAL, 59, 2704 (1937); Butenandt and Fleischer, *Ber.*, 68, 2094 (1935).



12(α)-Acetoxyprogesterone — *allo*-Pregnan-3,12,20-trione

12(α)-Hydroxypregnan-3,20-dione — Pregnan-3,12,20-trione

to lead to the *allo*-configuration at C-5. Nevertheless, we have prepared the corresponding isomer, pregnan-3,12,20-trione (IV), by the mild oxidation of an authentic sample of 12(α)-hydroxypregnan-3,20-dione (III). It had the following properties: m.p. 204–206°, $[\alpha]^{26}D$ +181°, $[\alpha]^{26}_{5461}$ +225° (chloroform). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.3; H, 9.2. Found: C, 76.0; H, 9.1. Reichstein and von Arx[5] report for pregnan-3,12,20-trione: m.p. 201–202°; $[\alpha]^{17}D$ +182 ± 7, $[\alpha]^{17}_{5461}$ +219 ± 8 (ethanol). A mixture of IV with II showed a melting point depression of 36°. The melting point of each of these compounds was depressed 10–20° by the trione from hecogenin.

Since the properties of *allo*-pregnan-3,12,20-trione (II) are different from those of the samples derived from hecogenin and botogenin, some doubt must be entertained as to the structures of the degradation products from both of these sapogenins.

We thank Parke, Davis and Company for their help.

(5) Reichstein and von Arx, *Helv. Chim. Acta*, **23**, 747 (1940).

THE WHITMORE LABORATORIES
SCHOOL OF CHEMISTRY AND PHYSICS — R. B. WAGNER
THE PENNSYLVANIA STATE COLLEGE — JAMES A. MOORE
STATE COLLEGE, PENNSYLVANIA — ROBERT F. FORKER

RECEIVED OCTOBER 10, 1949

SYNTHESES IN THE DIRECTION OF MORPHINE. I. 7-METHOXY- AND 7,8-DIMETHOXY-2-TETRALONE.

Sir:

We wish to report the synthesis of 7,8-dimethoxy-2-tetralone, which may serve as a useful intermediate for elaboration in the direction of morphine and certain of its degradation products,[1] and may open a way for the preparation of physiologically active substances oxygenated at points corresponding to the 3 and 4 positions in morphine. 7-Methoxy-2-tetralone may serve in the syntheses of substances similarly substituted in the 3 position; and is of particular interest in view of the recent report that 3-hydroxymorphinane is a powerful analgesic surpassing morphine in clinical tests[2].

1,2,7-Trimethoxynaphthalene,[3] m.p. 38.5–39.5°, b.p. 133° at 1 mm. (picrate[3], m.p. 113°), gave by reduction[4] with sodium and alcohol, the crystalline ketone, m.p. 76° (*anal.* calcd. for $C_{10}H_8O(OCH_3)_2$: OCH_3, 30.1. Found: OCH_3, 29.5, 29.3), characterized as the semicarbazone, m.p. 191–191.5°, and the 2,4-dinitrophenylhydrazone, m.p. 167° dec. (*anal.* calcd. for $C_{18}H_{18}O_8N_4$: C, 56.0; H, 4.7; N, 14.5. Found: C, 55.7; H, 4.6; N, 15.0, 14.8). The structure of the ketone was shown by oxidation, with alkaline permanganate, to hemipinic acid, identified by its m.p.[5] (177–179°) and by the m.p.[6] (166–167°) and characteristic fluorescence[6] of the pure anhydride.

2,7-Dimethoxynaphthalene similarly[4] gave on reduction 7-methoxy-2-tetralone, m.p. 27–28°, b.p. 124–126° (1.5 mm.); semicarbazone, m.p. 174–176° (*anal.* calcd. for $C_{12}H_{15}O_2N_3$: C, 61.8; H, 6.5. Found: C, 62.1, 62.1; H, 6.4, 6.4); 2,4-dinitrophenylhydrazone m.p. 177–181° (*anal.* calcd. for $C_{17}H_{16}N_4O_5$: C, 57.3; H, 4.5. Found: C, 57.2, 57.5; H, 4.4, 4.6).

(2) Schnider and Grussner, *Helv. Chim. Acta*, **32**, 821 (1939).
(3) Chakravarti and Pasupati, *J. Chem. Soc.*, 1859 (1937).
(4) Cornforth, Cornforth and Robinson, *ibid.*, 689 (1942).
(5) Perkin, *ibid.*, **109**, 922 (1916).
(6) Dobbie and Lauder, *ibid.*, **67**, 19 (1895).

DEPARTMENT OF CHEMISTRY — MILTON D. SOFFER
SMITH COLLEGE — J. CHARLES CAVAGNOL
NORTHAMPTON, MASS. — HILDA E. GELLERSON

RECEIVED OCTOBER 19, 1949

DEGRADATION OF GLYCOGEN TO ISOMALTOSE

Sir:

Methylation studies[1] have indicated that the glycogen molecule has a highly ramified structure composed of α-D-glucopyranosyl units joined 1,4 with branching at C6 on one out of twelve units. As additional evidence in support of this structure we report the isolation of crystalline 6-α-D-glucopyranosyl-β-D-glucopyranose octaacetate (β-D-isomaltose octaacetate)[2] from an acetylated acid hydrolysate of glycogen.

Animal (rabbit liver) glycogen (5.00 g., $[\alpha]^{25}D$ +200°, *c* 0.92, water) in 2% concentration was hydrolyzed at 100° in 0.05 *N* sulfuric acid for nine hours (degree of hydrolysis *ca.* 75%). After acid neutralization with barium carbonate and ion removal with exchange resins (Amberlite IR-100 and IR-4), the amorphous solid obtained on solvent removal was acetylated with hot acetic anhydride and sodium acetate. The resultant sugar acetate mixture (6.08 g.) was chromatographed[2] on Magnesol–Celite under such developmental conditions that monosaccharides were removed from the column. β-D-Glucose pentaacetate was identified,

(1) Fieser and Holmes, THIS JOURNAL, **60**, 2548 (1938); **58**, 2319 (1936); Cahn, *J. Chem. Soc.*, 2565 (1926).

(1) W. N. Haworth and E. G. W. Percival, *J. Chem. Soc.*, 2277 (1931); W. N. Haworth, E. L. Hirst and F. Smith, *ibid.*, 1914 (1939).
(2) M. L. Wolfrom, L. W. Georges and I. L. Miller, THIS JOURNAL, **69**, 473 (1947); **71**, 125 (1949).