most part those found to give the most active antispasmodics.[1,3]

Preliminary pharmacological studies indicate that some of these compounds are among the most potent antispasmodics, so far reported, having an activity approximately equal to that of atropine sulfate. These results are listed in Table I.

KALAMAZOO, MICHIGAN RECEIVED OCTOBER 25, 1951

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF SYNTEX, S. A.]

Steroidal Sapogenins. XVI.[1a] Introduction of the 11-Keto and 11α-Hydroxy Groups into Ring C Unsubstituted Steroids (Part 3).[1b] 11-Oxygenated Sapogenins

BY CARL DJERASSI,[2] E. BATRES,[2] M. VELASCO AND G. ROSENKRANZ

The structure of 9α,11α-oxido-22-isoallospirostan-3β-ol-7-one acetate (IIa), the performic acid oxidation product of the corresponding $\Delta^{7,9(11)}$-diene I, was proved by converting it *via* the 7-cycloethylenemercaptol to the known 9α,11α-oxido-22-isoallospirostan-3β-ol acetate (IIc). Alkaline isomerization of the epoxyketone IIa led to $\Delta^{8(9)}$-22-isoallospirosten-3β,11α-diol-7-one (III), which after hydrogenation and Huang-Minlon reduction afforded 22-isoallospirostan-3β,11α-diol (Va). Oxidation to the corresponding 3,11-dione (Vc), followed by Raney nickel hydrogenation gave 22-isoallospirostan-3β-ol-11-one (Vd), while lithium aluminum hydride treatment of the dione yielded 22-isoallospirostan-3β,11β-diol (Vf). These experiments complete the partial synthesis of the three possible C-11 oxygenated 22-isoallospirostan-3β-ols from the abundant plant sapogenin, diosgenin. Lithium aluminum hydride reduction of 9α,11α-oxido-22-isoallospirostan-3β-ol-7-one acetate (IIa) affected only the 7-keto group and oxidation of the reduction product VIa followed by alkaline isomerization gave $\Delta^{8(9)}$-22-isoallospirosten-3,7-dione-11α-ol (VIIa), which was correlated with the original epxoyketone isomerization product IIIa by oxidation to $\Delta^{8(9)}$-22-isoallospirosten-3,7,11-trione (VIIc). Selective reduction of the 3-keto group of the latter produced $\Delta^{8(9)}$-22-isoallospirosten-3β-ol-7,11-dione acetate (VIII), which could also be obtained by the Fieser dichromate oxidation of $\Delta^{7,9(11)}$-22-isoallospirostadien-3β-ol acetate (I). Zinc dust reduction of the unsaturated diketone VIII yielded 22-isoallospirostan-3β-ol-7,11-dione acetate (IX).

C-11 oxygenated steroidal sapogenins represent almost ideal starting materials for the partial synthesis of cortisone and related adrenal steroids, but until now no such representative in the sapogenin series has been isolated from plant sources. The present paper is concerned with the partial synthesis of 11-keto (Vd), 11α-hydroxy (Va) and 11β-hydroxy (Vf) 22-isoallospirostan-3β-ols[3] from the abundant, ring C unsubstituted sapogenin Δ^5-22-isospirosten-3β-ol (diosgenin). The publication of the physical constants of the three 11-oxygenated 22-isoallospirostan-3β-ols (Va, d, f) should facilitate the identification of such sapogenins in the event that they should be encountered subsequently in plant sources. Furthermore, the presently described experiments represent an alternate route from diosgenin to cortisone, since 22-isoallospirostan-3β-ol-11-one (Vd), which has previously been synthesized from 22-isoallospirostan-3β-ol-12-one[1a] (hecogenin) as well as from diosgenin,[4] has already been transformed[4-7] into cortisone.

It has been reported[8] earlier from this Laboratory that performic acid oxidation of $\Delta^{7,9(11)}$-22-isoallospirostadien-3β-ol acetate (I)[9] affords 9α,11α-oxido-22-isoallospirostan-3β-ol-7-one acetate (IIa) and the structure of this key intermediate has now been proved through correlation with the known[10] 9α,11α-oxido-22-isoallospirostan-3β-ol acetate (IIc) by means of Raney nickel desulfurization of the 7-cycloethylenemercaptol IIb. The subsequent transformations of this epoxyketone IIa, which serve as additional structure proof, proceeded exactly as described[2,8] in the allopregnane series: alkaline isomerization led to $\Delta^{8(9)}$-22-isoallospirosten-3β,11α-diol-7-one (IIIa), which was hydrogenated[11] to the saturated 3β,11α-diol-7-one (IVa) and reduced by the Huang-Minlon[12] procedure to the desired 22-isoallospirostan-3β,11α-diol (Va). The spectral data of these intermediates, reported in the experimental section, fully support the structure assignments, while the α-configuration of the C-11 hydroxyl group (in IIIa, IVa and Va), and *ipso facto* of the 9,11-epoxide ring (in IIa, b, c), was demonstrated by the ease of acetylation (IIIb, IVb, Vb), characteristic[13] of the 11α- but not the 11β-hydroxy series.

The other two C-11 oxygenated 22-isoallospirostan-3β-ols (Vd, Vf) were prepared by unexceptional methods. The 3β,11α-diol Va was oxidized to 22-isoallospirostan-3,11-dione (Vc) and then hydrogenated with Raney nickel catalyst at room temperature, conditions which are not sufficient to reduce the C-11 keto group, to yield 22-isoallospirostan-3β-ol-11-one (Vd), identical with a specimen prepared[1a] from 22-isoallospirostan-3β-ol-12-one (hecogenin). An alternate synthesis of this 11-ketone Vd from diosgenin has already been re-

(1a) Paper XV, C. Djerassi, H. J. Ringold and G. Rosenkranz, THIS JOURNAL, **73**, 5513 (1951).

(1b) Part 2, C. Djerassi, O. Maucera, G. Stork and G. Rosenkranz, *ibid.*, **73**, 4496 (1951).

(2) Department of Chemistry, Wayne University, Detroit, Michigan.

(3) For nomenclature of steroidal sapogenins see G. Rosenkranz and C. Djerassi, *Nature*, **166**, 104 (1950). *Cf.* Report of Steroid Nomenclature Committee, *Helv. Chim. Acta*, **34**, 1680 (1951).

(4) E. M. Chamberlain, W. V. Ruyle, A. E. Erickson, J. M. Chemerda, L. M. Aliminosa, R. L. Erickson, G. E. Sita and M. Tishler, THIS JOURNAL, **73**, 2396 (1951).

(5) G. Rosenkranz, J. Pataki and C. Djerassi, *ibid.*, **73**, 4055 (1951).

(6) G. Rosenkranz, C. Djerassi, R. Yashin and J. Pataki, *Nature*, **168**, 28 (1951).

(7) J. M. Chemerda, E. M. Chamberlain, E. H. Wilson and M. Tishler, THIS JOURNAL, **73**, 4053 (1951).

(8) G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 3546 (1951).

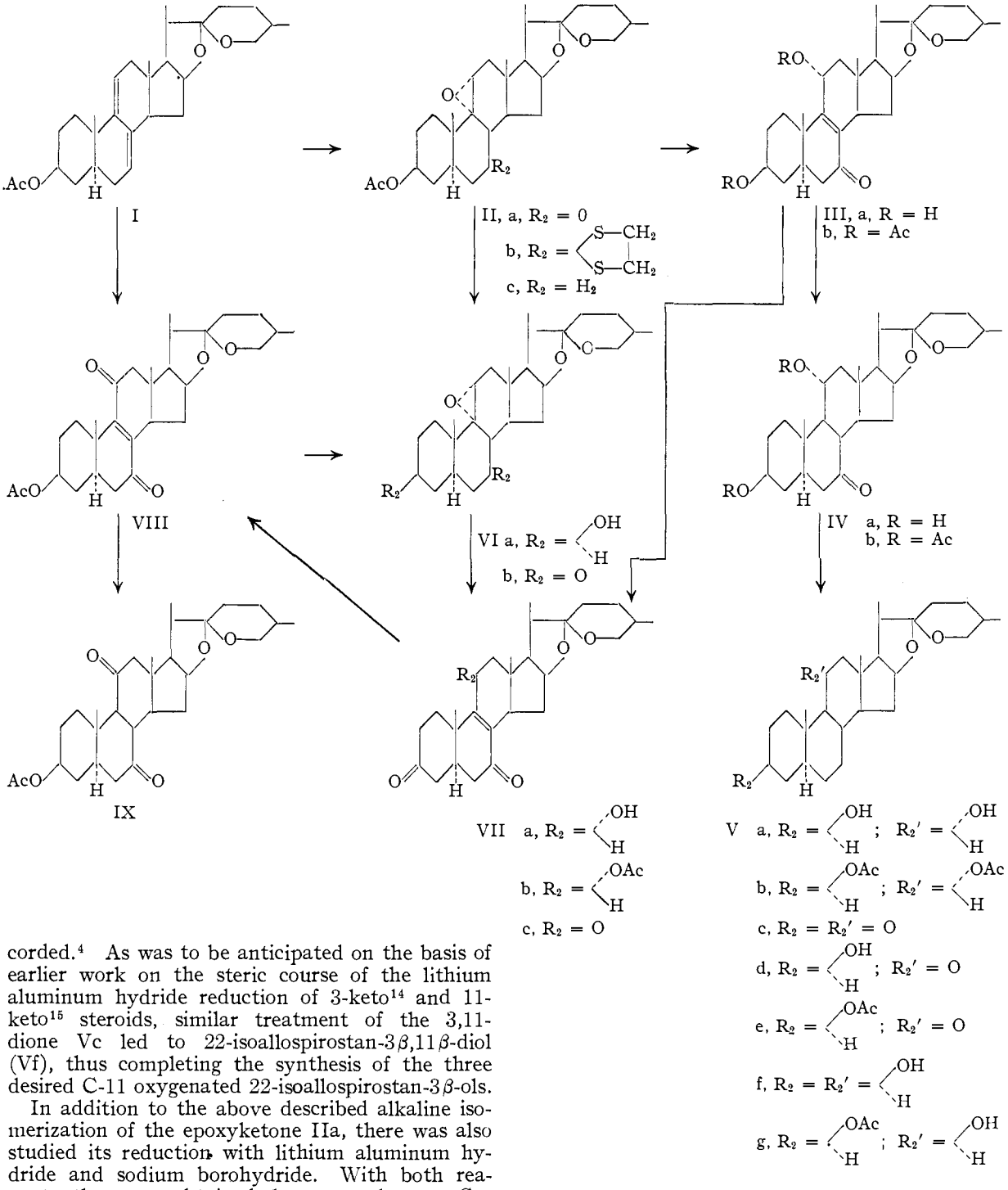
(9) The synthesis of this diene (I) from diosgenin has already been described [G. Rosenkranz, J. Romo, E. Batres and C. Djerassi, *J. Org. Chem.*, **16**, 298 (1951)].

(10) C. Djerassi, H. Martinez and G. Rosenkranz, *ibid.*, **16**, 1278 (1951).

(11) The smooth hydrogenation (palladized charcoal catalyst, room temperature, atmospheric pressure) is noteworthy if viewed in the light of the known resistance [*cf.* D. H. R. Barton and J. D. Cox, *J. Chem. Soc.*, 214 (1949)] of $\Delta^{8(9)}$-stenols toward reduction, and indicates that it may possibly proceed through an enol form.

(12) Huang-Minlon, THIS JOURNAL, **71**, 3301 (1949).

(13) W. P. Long and T. F. Gallagher, *J. Biol. Chem.*, **162**, 511 (1946).



corded.[4] As was to be anticipated on the basis of earlier work on the steric course of the lithium aluminum hydride reduction of 3-keto[14] and 11-keto[15] steroids, similar treatment of the 3,11-dione Vc led to 22-isoallospirostan-3β,11β-diol (Vf), thus completing the synthesis of the three desired C-11 oxygenated 22-isoallospirostan-3β-ols.

In addition to the above described alkaline isomerization of the epoxyketone IIa, there was also studied its reduction with lithium aluminum hydride and sodium borohydride. With both reagents, there was obtained the same substance $C_{27}H_{42}O_5$, to which is assigned the structure 9α,11α-oxido-22-isoallospirostan-3β,7(β?)-diol (VIa) and which was oxidized to 9α,11α-oxido-22-isoallospirostan-3,7-dione (VIb). The presence of the intact oxide function[16] in VIa and b was demonstrated by the characteristic alkaline isomerization (*cf.* IIa→IIIa) of 9α,11α-oxido-22-isoallospirostan-3,7-dione (VIb) (no ultraviolet absorption maximum) to $\Delta^{8(9)}$-22-isoallospirosten-11α-ol-3,7-dione (VIIa) (ultraviolet absorption maximum at 254 mμ, typical of $\Delta^{8(9)}$-7-ketones), further characterized by formation of the 11α-acetate VIIb. The structure proof was completed by chromium trioxide oxidation of the unsaturated 3,7-dione-11α-ol VIIa to $\Delta^{8(9)}$-22-isoallospirosten-3,7,11-trione (VIIc), identical with a sample prepared by oxidation of $\Delta^{8(9)}$-22-isoallospirosten-3β,11α,diol-7-one (IIIa). The unsaturated trione VIIc was hydro-

(14) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 687 (1950).

(15) L. H. Sarett, M. Feurer and K. Folkers, THIS JOURNAL, **73**, 1777 (1951); P. L. Julian, E. W. Meyer, W. J. Karpel and W. Cole, *ibid.*, **73**, 1982 (1951); C. Djerassi, G. Rosenkranz, J. Pataki and St. Kaufmann, *J. Biol. Chem.*, **194**, 115 (1952).

(16) Steroidal 9α,11α-oxides are not attacked by lithium aluminum hydride (*cf.* ref. 10, and L. F. Fieser and S. Rajagopalan, THIS JOURNAL, **73**, 118 (1951).

genated selectively at C-3 to afford, after acetylation, $\Delta^{8(9)}$-22-isoallospirosten-3β-ol-7,11-dione acetate (VIII), which could also be obtained in 4% yield by the one-step dichromate oxidation[17] of $\Delta^{7,9(11)}$-22-isoallospirostadien-3β-ol acetate (I).[9] The synthesis of the $\Delta^{8(9)}$-7,11-dione VIII through VII represents the fifth route[1b,4,17,18] to such unsaturated diketones, which are reducible with zinc and acetic acid[4,17,18] to the saturated 7,11-diketones, the penultimate intermediates in a number of 11-ketosteroid syntheses.[4,17,18,18a] The specific application of the zinc dust reduction to the sapogenin derivative VIII is described in the experimental section and led in *ca.* 50% yield to 22-isoallospirostan-3β-ol-7,11-dione acetate (IX).

Experimental[19]

9α,11α-Oxido-22-isoallospirostan-3β-ol-7-cycloethylenemercaptol 3-Acetate (IIb).[20]—9α,11α-Oxido-22-isoallospirostan-3β-ol-7-one acetate (IIa)[8] (0.8 g.) was converted in 72% yield into the mercaptol IIb by Hauptmann's method,[21] employing 40 cc. of dry dioxane, 1 cc. of ethanedithiol, 8 g. of anhydrous sodium sulfate and 8 g. of anhydrous zinc chloride for 18 hours at room temperature. The analytical sample crystallized from chloroform–methanol as colorless needles with m.p. 288–290, $[\alpha]^{20}D$ −86° (dioxane).

Anal. Calcd. for $C_{31}H_{46}O_5S_2$: C, 66.16; H, 8.23; S, 11.37. Found: C, 66.19; H, 8.50; S, 11.80.

9α,11α-Oxido-22-isoallospirostan-3β-ol Acetate (IIc).[20]—The mercaptol (0.4 g.) was desulfurized by refluxing with 300 cc. of ethanol and 10 g. of W-2 Raney nickel catalyst for three hours, filtering the catalyst and evaporating to dryness. Recrystallization from chloroform–methanol afforded 0.21 g. of the oxide IIc with m.p. 246–250°, $[\alpha]^{20}D$ −65.3°, which gave no depression in m.p. upon admixture with an authentic sample[10] (reported m.p. 248–252°, $[\alpha]^{20}D$ −65°).

$\Delta^{8(9)}$-22-Isoallospirosten-3β,11α-diol-7-one (IIIa).—A suspension of 10 g. of the epoxyketone IIa[8] in 2 l. of methanol was refluxed for 30 minutes with 7 g. of potassium carbonate and 400 cc. of water, whereupon a homogeneous solution was obtained. After concentrating to a volume of 1 l., diluting with ice-water and filtering, there was isolated 9.2 g. of colorless crystals with m.p. 205–213°. Recrystallization from acetone raised the m.p. to 215–216°, $[\alpha]^{20}D$ −27°, $\lambda_{max.}^{EtOH}$ 252 mμ, log ϵ 4.08, $\lambda_{max.}^{nujol}$ 1656 cm.$^{-1}$ and free hydroxyl band.

Anal. Calcd. for $C_{27}H_{40}O_5$: C, 72.94; H, 9.07. Found: C, 73.08; H, 9.17.

The diacetate IIIb after recrystallization from hexane–acetone showed m.p. 171–172°, $[\alpha]^{20}D$ + 4°, $\lambda_{max.}^{EtOH}$ 251 mμ, log ϵ 4.04, $\lambda_{max.}^{CS_2}$ 1736 (acetate) and 1676 cm.$^{-1}$ (Δ^8-7-ketone), no free hydroxyl band.

Anal. Calcd. for $C_{31}H_{44}O_7$: C, 70.43; H, 8.39. Found: C, 70.55; H, 8.51.

22-Isoallospirostan-3β,11α-diol-7-one (IVa).—A solution of 1.9 g. of the unsaturated diol IIIa in 150 cc. of ethanol or ethyl acetate was shaken in an atmosphere of hydrogen at room temperature and atmospheric pressure with 0.4 g. of 10% palladized charcoal catalyst (American Platinum Works, Newark, N.J.) for two hours, at which time the gas uptake corresponded to one mole. Filtration of the catalyst, evaporation of the filtrate to dryness and recrystallization from ethyl acetate afforded 1.27 g. of the saturated diol IVa with m.p. 236–237°, $[\alpha]^{20}D$ −137°, $\lambda_{max.}^{CHCl_3}$ 1702 cm.$^{-1}$ (saturated 7-ketone) and free hydroxyl band.

Anal. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48. Found: C, 72.91; H, 9.35.

The diacetate IVb was recrystallized from ether–hexane; m.p. 225–227°, $[\alpha]^{20}D$ −96.7°.

Anal. Calcd. for $C_{31}H_{46}O_7$: C, 70.16; H, 8.74. Found: C, 70.21; H, 8.67.

22-Isoallospirostan-3β,11α-diol (Va).—A solution of 4.0 g. of the above 3,11-diol-7-one IVa in 150 cc. of ethylene glycol and 8 cc. of hydrazine hydrate was refluxed for one hour, cooled in ice, 9.0 g. of potassium hydroxide in 12 cc. of water was added and the mixture was distilled until the temperature of the vapor reached 190°. A reflux condenser was attached, the solution was refluxed for 4 hours, cooled, poured into ice-cold dilute hydrochloric acid solution and extracted with chloroform. The neutral and dry chloroform extract was evaporated to dryness and the residue crystallized from acetone; yield 2.27 g., m.p. 214–216°. Two additional recrystallizations from acetone furnished the analytical sample, m.p. 217–218°, $[\alpha]^{20}D$ −69°, which showed no carbonyl band in the infrared.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25. Found: C, 74.82; H, 10.47.

The diacetate Vb exhibited m.p. 175–177°, $[\alpha]^{20}D$ −84°; no free hydroxyl band in the infrared.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.06; H, 9.36. Found: C, 72.31; H, 9.49.

22-Isoallospirostan-3,11-dione (Vc).—The 3β,11α-diol Va was oxidized with sodium dichromate dihydrate in benzene-acetic acid solution[24] and the product crystallized from ether-hexane; m.p. 236–238°, $[\alpha]^{20}D$ −19°. The infrared spectrum ($CHCl_3$) showed a carbonyl band at 1704 cm.$^{-1}$ and was identical in every respect with that of a specimen of the dione Vc prepared from 22-isoallospirostan-3β-ol-12-one.[1a]

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.66; H, 9.41. Found: C, 75.35; H, 9.24.

22-Isoallospirostan-3β-ol-11-one (Vd).—A solution of 0.3 g. of the 3,11-dione Vc in 50 cc. of ethanol (distilled over Raney nickel) was shaken in an atmosphere of hydrogen at room temperature and atmospheric pressure with a small spoon full of prereduced W-4 Raney nickel catalyst[22] for one-half hour. Filtration of the catalyst, evaporation of the filtrate to dryness and recrystallization from acetone furnished 0.26 g. of the hydroxyketone Vd with m.p. 223–225°, $[\alpha]^{20}D$ −30°, $\lambda_{max.}^{CHCl_3}$ 1702 cm.$^{-1}$ and free hydroxyl band.

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.30; H, 9.83. Found: C, 75.16; H, 10.01.

The acetate Ve[23] exhibited m.p. 222–223°, $[\alpha]^{20}D$ −32° and proved to be identical (mixed m.p., infrared spectrum) with a sample prepared from 22-isoallospirostan-3β-ol-12-one.[1a]

22-Isoallospirostan-3β,11β-diol (Vf).—The lithium aluminum hydride reduction of the 3,11-dione Vc (0.3 g.) was carried out in the usual manner with 0.2 g. of lithium aluminum hydride in ether solution (45 minutes refluxing) and after recrystallization from hexane–ether yielded 0.19 g. of pure 3β,11β-diol with m.p. 202–204°, $[\alpha]^{20}D$ −49°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25. Found: C, 75.21; H, 10.06.

The 3-monoacetate Vg showed m.p. 225–227°, $[\alpha]^{20}D$ −47°, acetate as well as free hydroxyl bands in the infrared.

Anal. Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.19; H, 9.81.

9α,11α-Oxido-22-isoallospirostan-3β,7(β?)-diol (VIa).—The epoxyketone IIa (0.88 g.) was reduced (30 minutes refluxing) with 0.8 g. of lithium aluminum hydride in 100 cc.

(17) L. F. Fieser, J. E. Herz and W. Huang, *ibid.*, **73**, 2397 (1951).

(18) L. F. Fieser, J. C. Babcock, J. E. Herz, W. Huang and W. P. Schneider, *ibid.*, **73**, 4053 (1951).

(18a) ADDED IN PROOF.—Since this paper was submitted, H. Heusser, K. Eichenberger, P. Kurath, H. R. Dällenbach and O. Jeger [*Helv. Chim. Acta.*, **34**, 2106 (1951)] have described a further route to $\Delta^{8(9)}$-7,11-diones, which were also converted *via* the saturated 7,11-diones to 11-kestosteroids. [*Cf.* also H. Heusser, K. Heusler, K. Eichenberger, C. G. Honegger and O. Jeger, *ibid.*, **35**, 295 (1952)].

(19) All melting points are uncorrected. Unless noted otherwise, rotations were determined in chloroform and ultraviolet absorption spectra in 95% ethanol solution. We are grateful to Srta. Paquita Revaque for these measurements as well as for the infrared spectra, which were measured on a Perkin-Elmer model 12C spectrometer with sodium chloride prism. Thanks are due to Srta. Amparo Barba and staff for the microanalyses.

(20) This experiment was kindly performed by Dr. J. Romo of this Laboratory.

(21) H. Hauptmann, THIS JOURNAL, **69**, 562 (1947).

(22) A. Pavlic and H. Adkins, *ibid.*, **68**, 1471 (1946).

(23) Reference 4 records m.p. 224–229°, $[\alpha]^{20}D$ −39.4° for the acetate Ve.

of tetrahydrofuran. Recrystallization from acetone yielded 0.63 g. of the oxido-diol VIa with m.p. 237–239°, $[\alpha]^{20}D$ −66.5°, free hydroxyl band in the infrared. The identical product was obtained when the epoxyketone was reduced with sodium borohydride in methanol solution (30 minutes at 50°, 18 hours at room temperature).

Anal. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48. Found: C, 72.26; H, 9.40.

9α,11α-Oxido-22-isoallospirostan-3,7-dione (VIb).—One gram of the oxido-diol VIa in 100 cc. of benzene was treated at room temperature dropwise with stirring with a solution of 2.0 g. of sodium dichromate dihydrate[17] in 50 cc. of acetic acid and then left overnight. The usual work-up followed by recrystallization from acetone yielded 0.48 g. of pure oxido-dione VIb with m.p. 271–272.5°, $[\alpha]^{20}D$ −104°, $\lambda_{max.}^{EtOH}$ 286 mμ, log ε 1.85, $\lambda_{max.}^{nujol}$ 1716 cm.$^{-1}$, no free hydroxyl band.

Anal. Calcd. for $C_{27}H_{38}O_5$: C, 73.27; H, 8.65. Found: C, 73.55; H, 8.49.

$\Delta^{8(9)}$-22-Isoallospirosten-3,7-dione-11α-ol (VIIa).—The isomerization of the oxido-dione VIb (0.5 g.) was accomplished by refluxing for one hour with 0.4 g. of potassium hydroxide and 50 cc. of methanol. Recrystallization from chloroform–acetone produced 0.38 g. of colorless crystals with m.p. 262–264°, $[\alpha]^{20}D$ −23.6°, λ_{max}^{EtOH} 254 mμ, log ε 4.11, λ_{max}^{nujol} 1718 cm.$^{-1}$ (3-ketone), 1660 cm.$^{-1}$ (Δ^8-7-ketone) and free hydroxyl band.

Anal. Calcd. for $C_{27}H_{38}O_5$: C, 73.27; H, 8.65. Found: C, 73.72; H, 8.60.

The acetate VIIb was recrystallized from acetone, m.p. 216–218°, $[\alpha]^{20}D$ +11.7°.

Anal. Calcd. for $C_{29}H_{40}O_6$: C, 71.87; H, 8.32. Found: C, 71.71; H, 8.21.

$\Delta^{8(9)}$-22-Isoallospirosten-3,7,11-trione (VIIc) (a) From $\Delta^{8(9)}$-22-Isoallospirosten-3,7-dione-11α-ol (VIIa).—Chromium trioxide (0.25 g.) oxidation at 15° for two hours in 50 cc. of acetic acid of 0.6 g. of the dione VIIa afforded after recrystallization from chloroform–ether 0.31 g. of yellowish crystals of the triketone with m.p. 243–245°, $[\alpha]^{20}D$ −3°, $\lambda_{max.}^{EtOH}$ 268 mμ, log ε 3.95, $\lambda_{max.}^{CHCl_3}$ 1715 and 1682 cm.$^{-1}$, no free hydroxyl band. The ultraviolet absorption maximum at 268 mμ is characteristic[1b,4,17,18] of the Δ^8-7,11-dione moiety.

Anal. Calcd. for $C_{27}H_{36}O_5$: C, 73.60; H, 8.24. Found: C, 73.53; H, 8.52.

(b) **From $\Delta^{8(9)}$-22-Isoallospirosten-3-β,11α-diol-7-one (IIIa).**—When carried out as in (a), 1.0 g. of IIIa yielded 0.47 g. of yellowish trione VIIc, identical in all respects (including infrared spectrum) with the material prepared from VIIa.

$\Delta^{8(9)}$-22-Isoallospirosten-3β-ol-7,11-dione Acetate (VIII) (a) By Sodium Dichromate Oxidation of $\Delta^{7,9(11)}$-22-Isoallospirostadien-3β-ol Acetate (I).—Four grams of the diene I[9] in 80 cc. of benzene was oxidized overnight by the general procedure of Fieser, Herz and Huang[17,24] with 7.0 g. of sodium dichromate dihydrate in 80 cc. of acetic acid. The total oxidation product was subjected to a Girard separation and the ketonic fraction (0.8 g.) was chromatographed on 40 g. of ethyl acetate-washed alumina. The eluates possessing an ultraviolet absorption maximum at 266–270 mμ were combined and recrystallized from methanol, affording 0.15 g. (4%) of yellowish crystals with m.p. 212–215°, $[\alpha]^{20}D$ −22°, $\lambda_{max.}^{EtOH}$ 270 mμ, log ε 3.97, $\lambda_{max.}^{CS_2}$ 1736 (acetate) and 1686 cm.$^{-1}$ (Δ^8-7,11-dione system).

Anal. Calcd. for $C_{29}H_{40}O_6$: C, 71.87; H, 8.32. Found: C, 71.73; H, 8.60.

(b) **By Raney Nickel Reduction of $\Delta^{8(9)}$-22-Isoallospirosten-3,7,11-trione (VIIc).**—The selective hydrogenation of 2.0 g. of the unsaturated trione VIIc was carried out exactly as described above for the Raney nickel reduction of Vc to Vd. The yellowish hydrogenation product was acetylated with pyridine–acetic anhydride and chromatographed on ethyl acetate-washed alumina as described under (a). Recrystallization gave 0.94 g. of the yellowish dione acetate VIII with m.p. 213–214°, $[\alpha]^{20}D$ −18°, $\lambda_{max.}^{EtOH}$ 270 mμ, log ε 3.95. The infrared spectrum was identical with that of the sample prepared according to (a).

22-Isoallospirostan-3β-ol-7,11-dione Acetate (IX).—A solution of 0.5 g. of the unsaturated dione VIII in 50 cc. of acetic acid was stirred for 3 hours on the steam-bath with 2.5 g. of zinc dust. After filtering, removing the acetic acid *in vacuo*, chromatographing the residue on 20 g. of ethyl acetate-washed alumina and recrystallizing from acetone, there was obtained 0.245 g. of colorless crystals of the saturated dione IX with m.p. 234–236°, $[\alpha]^{20}D$ −76°, $\lambda_{max.}^{CS_2}$ 1736 and 1716 cm.$^{-1}$.

(24) *Cf.* L. F. Fieser, THIS JOURNAL, **73**, 5007 (1951).

MEXICO CITY 17, D. F. RECEIVED OCTOBER 8, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Acyl Derivatives of D-Glucosaminic Acid

BY M. L. WOLFROM AND M. J. CRON[1]

Improved preparative directions are recorded for D-glucosamine hydrochloride and for D-glucosaminic acid (I). Schotten–Baumann benzoylation of I gave tetra-O-benzoyl-D-glucosaminic acid (V). Treatment of I successively with alkali and acetic anhydride, liquid ammonia and then acetic anhydride and pyridine, gave 2,3,4,5,6-pentaacetyl-D-glucosaminamide (IV) which on deamination yielded pentaacetyl-D-glucosaminic acid (VI).

Aldonic acids containing a free carboxyl group and having all hydroxyl functions esterified with a simple carboxylic acid are well established derivatives that are useful in synthesis.[2–5] The corresponding substances in the 2-amino-2-desoxyaldose series are unknown and were desired for further synthetic work. We describe herein the preparation in crystalline form of several such acyl derivatives of D-glucosaminic acid.

Improved preparative directions are recorded herein for the depolymerization of chitin to D-glucosamine hydrochloride and for its oxidation to D-glucosaminic acid (I). A Schotten–Baumann benzoylation of the latter led to the formation in low yield (4%) of tetra-O-benzoyl-D-glucosaminic acid (V). Karrer and Mayer[6] had prepared crystalline N-acetyl-D-galactosaminic lactone by acetylation of its sodium salt in aqueous solution followed by treatment with mineral acid. Application of this technique to D-glucosaminic acid yielded an uncharacterized amorphous product (presumably II) that was treated with liquid ammonia according to the general procedure of Glattfeld and MacMillan.[7] The crude amorphous substance

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