Ethyl m-[bis(2-chloroethyl)amino]phenoxy acetate (VIII). A mixture of 1.0 g. (3.5 mmoles) of ethyl *m*-[bis(2-hydroxyethyl)amino]phenoxy acetate (X) and 7.5 ml. of freshly distilled phosphorus oxychloride was refluxed for 15 min. The green-colored solution was poured into 100 ml. of ice and stirred well for 10 min. The mixture was neutralized with sodium acetate to *p*H 5 and extracted with 100 ml. of dichloromethane. The extract was washed with 50 ml. of water, dried over anhydrous magnesium sulfate, then concentrated *in vacuo* to yield a yellow-green oil. This oil was dissolved in 10 ml. of dichloromethane and 50 ml. of toluene and evaporated to dryness (bath 50°) *in vacuo* to remove acetic acid. The residue oil crystallized upon standing; yield, 1.0 g. (88%), m.p. 38–39°; $\lambda_{max(\mu)}^{film}$ 5.63 (ester C=O); 8.30, 8.56 (ester C—O—C); 13.30 (*m*-disubstituted benzene); free of COH near 3.0 and 9.5. The compound traveled as a single spot (R_f 0.52) in System A.[13]

Anal. Calcd. for $C_{14}H_{19}Cl_2NO_3$: C, 52.5; H, 5.95; Cl, 22.2. Found: C, 52.3; H, 6.29; Cl, 22.1.

Ethyl 3-{m-[bis(2-chloroethyl)amino]phenoxy}propionate (IX). The chlorination of 1.0 g. (3.0 mmoles) of ethyl 3-{*m*-[bis(2-hydroxyethyl)amino]phenoxy}propionate (XI) was performed in essentially the same manner as described for X except that XI was heated for 30 min. with phosphorus oxychloride on a steam bath, rather than refluxed for 15 min. The product (IX), after crystallization from ether-petroleum ether (b.p. 30–60°), was obtained in 96% yield, m.p. 31–32°; $\lambda_{max(\mu)}^{Nujol}$ 5.78 (ester C=O); 8.40, 8.60 (ester C—O—C); 13.32 (*m*-disubstituted benzene); 13.90 (C—Cl); absence of OH near 3.0 and 9.5. The compound traveled as a single spot (R_f 0.61) in System A.[13]

Anal. Calcd. for $C_{15}H_{21}Cl_2NO_3$: C, 53.9; H, 6.29; Cl, 21.3. Found: C, 54.1; H, 6.49; Cl, 21.5.

Ethyl 3-{o-[bis(2-chloroethyl)amino]phenoxy}propionate (XVI). Treatment of 1.0 g. (3.0 mmoles) of ethyl 3-{*o*-[bis-(2-chloroethyl)amino]phenoxy}propionate (XVIII) with phosphorus oxychloride in the same manner as for X yielded 0.95 g. (82%) of a light amber oil which crystallized to fine needles melting below 20°; $\lambda_{max(\mu)}^{film}$ 5.72 (ester C=O); 8.42 (ester C—O—C); 13.30 (*o*-disubstituted benzene); 13.90 (C—Cl); absence of OH near 3.0 and 9.5. The compound traveled as a single spot (R_f 0.71) in System A,[13] and analysis showed it was nearly pure.

Anal. Calcd. for $C_{15}H_{21}Cl_2NO_3$: C, 53.9; H, 6.29; Cl, 21.3; N, 4.19. Found: C, 54.7; H, 6.53; Cl, 20.7; N, 4.34.

{m-[Bis(2-chloroethyl)amino]phenoxy}acetic acid (VI). A solution of 0.10 g. (0.30 mmole) of ethyl {*m*-[bis(2-chloroethyl)amino]phenoxy}acetate (VIII) in 2 ml. of concd. hydrochloric acid was refluxed for 10 min., cooled, and neutralized with sodium acetate to *p*H 5. The product was extracted with 25 ml. of dichloromethane; the extract was washed with 10 ml. of water, dried over anhydrous magnesium sulfate, then concentrated to dryness *in vacuo*. The white solid was dissolved in toluene and again concentrated *in vacuo* to yield 0.080 g. (87%) of white crystals m.p. 127–128°; $\lambda_{max(\mu)}^{Nujol}$ 3.50–4.00 (acidic OH); 5.72 (carboxyl C=O); 13.28 (*m*-disubstituted benzene); 13.45 (C—Cl). The compound traveled as a single spot (R_f 0.87) in System B.[13]

Anal. Calcd. for $C_{12}H_{15}Cl_2NO_3$: C, 49.3; H, 5.14; Cl, 24.3. Found: C, 49.6; H, 5.43; Cl, 24.4.

3-{m-[Bis(2-chloroethyl)amino]phenoxy}propionic acid (VII). The hydrolysis of 0.90 g. (3.0 mmoles) of ethyl 3-{*m*-[bis(2-chloroethyl)amino]phenoxy}propionate (IX) was carried out in the same manner as was that of VIII except that the time of reflux was lengthened to 30 min. An 88% yield of product, m.p. 134–136°, was obtained. Recrystallization from petroleum ether (b.p. 30–60°) gave an analytical sample, m.p. 138–139°; $\lambda_{max(\mu)}^{Nujol}$ 3.50–4.00 (acidic OH); 5.83 (carboxy C=O); 13.30 (*m*-disubstituted benzene); 13.90 (C—Cl); absence of OH near 3.0. The compound traveled as a single spot (R_f 0.70) on paper in System A.[13]

Anal. Calcd. for $C_{13}H_{17}Cl_2NO_3$: C, 51.0; H, 5.55; Cl, 23.2; N, 4.57. Found: C, 51.1; H, 5.62; Cl, 23.1; N, 4.75.

3-{o-[Bis(2-chloroethyl)amino]phenoxy}propionic acid (XV). Hydrolysis of 0.50 g. (1.5 mmoles) of ethyl 3-{*o*-[bis-(2-chloroethyl)amino]phenoxy}propionate (XVI) with concd. hydrochloric acid in the same manner as described for VIII yielded 0.40 g. (87%) of crystalline product, m.p. 65–67°. Recrystallization from petroleum ether (b.p. 30–60°) yielded an analytical sample, m.p. 71.5–73°; $\lambda_{max(\mu)}^{Nujol}$ 3.80–4.20 (acidic OH); 5.80 (carboxyl C=O); 13.00 (*o*-disubstituted benzene); 13.89 (C—Cl). The compound traveled as a single spot (R_f 0.77) in System A.[13]

Anal. Calcd. for $C_{13}H_{17}Cl_2NO_3$: C, 51.0; H, 5.56; Cl, 23.2; N, 4.57. Found: C, 50.9; H, 5.60; Cl, 22.9; N, 4.61.

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MENLO PARK, CALIF.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

Chiapagenin and Isochiapagenin. Two New Steroidal Sapogenins from *Dioscorea chiapasensis*[1]

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Dioscorea chiapasensis Matuda was found to contain diosgenin, yamogenin, correlogenin (neobotogenin), and two new dihydroxy sapogenins, now named chiapagenin and isochiapagenin. Chiapagenin was shown to be 12β-hydroxyyamogenin by appropriate interconversions with correlogenin and with sisalagenin. Isochiapagerin has been identified as 12β-hydroxydiosgenin.

During the past few years relatively few new steroidal sapogenins have been isolated, most of them being C-1 hydroxylated steroids (*e.g.*, ruscogenin, rhodeasapogenin, tokorogenin, kogagenin).[3] Of particular interest is the recent report by

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(2) Research Laboratories, Syntex, S.A., Mexico, D. F.

(3) For detailed review and references on these and other steroidal sapogenins see L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, 1959, chap. 21.

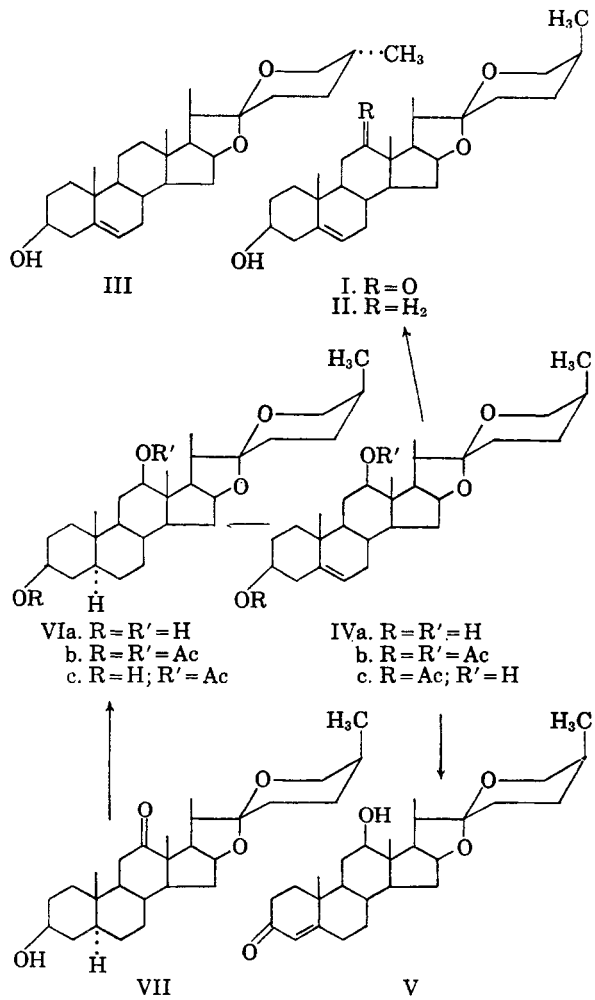
Takeda and Hamamoto[4] that metagenin represents an 11-hydroxylated sapogenin, thus demonstrating for the first time that sapogenins oxygenated at the important 11 position may be encountered in nature. This encouraged us to examine in detail *Dioscorea chiapasensis* Matuda, since this species has not been included among the 5000 plants covered in the U.S.D.A. sapogenin survey[5] and since preliminary work had indicated the presence of several sapogenins.[6]

The crude sapogenin mixture obtained on acid hydrolysis of the alcoholic extract of *D. chiapasensis* was first subjected to treatment with Girard's reagent T, since infrared examination of the crude mixture indicated the presence of some ketonic material. Chromatography of the ketonic fraction from the Girard fractionation led to a small amount of pure correlogenin (neobotogenin) (I).[7]

Most of the material appeared in the "nonketonic" fraction and since this did not exhibit any carbonyl absorption in the infrared, it could not contain any 11-ketosapogenin, which presumably would have appeared in the "nonketonic" portion. Chromatography effected separation into two principal components, which on the basis of their order of elution were judged to contain, respectively, mono and dihydroxylated sapogenins. The monohydroxy sapogenins were acetylated and rechromatographed, whereupon it could be demonstrated that they consisted of a mixture of yamogenin (II) and diosgenin (III).

The single largest component of the steroidal sapogenin mixture was represented by the dihydroxy fraction, which crystallized readily to afford a pure sapogenin $C_{27}H_{42}O_4$, m.p. 257–259°, $[\alpha]_D$ −130°, characterized further by its diacetate m.p. 194–196°, $[\alpha]_D$ −128°. Inspection of the literature[3] showed that this was a new sapogenin and we have, therefore, named it "chiapagenin" in accordance with its botanical origin.

The infrared spectrum of chiapagenin exhibited bands characteristic[8] of the "neo" series and since its optical rotation was typical[8] of Δ^5-steroidal sapogenins, one could conclude tentatively that chiapagenin is *x*-hydroxyyamogenin. The second hydroxyl group could not be located at positions 2 or 4, because chiapagenin did not consume any lead tetraacetate under conditions where such dihydroxy sapogenins react readily.[9] Positions 1 (*i.e.*, neoruscogenin)[10] and 7 were excluded by the course of the Oppenauer oxidation, which led to a monohydroxy Δ^4-3-ketone (V), without elimination of the second hydroxyl function, as might be expected if the latter were situated at C-1 or C-7. The formation of V confirmed the presence of a Δ^5-3-hydroxy system and this left only C-11, C-12, or C-15 as possible nuclear points of attachment for the other alcoholic function, tertiary positions being excluded by formation of chiapagenin diacetate; this problem seemed, therefore, most readily resolvable by selective oxidation of this second hydroxyl group. If the resulting ketone were not identical with correlogenin (I), then the



(4) K. Takeda and K. Hamamoto, *Tetrahedron Letters*, *No.* 3, 1 (1960).

(5)(a) M. E. Wall, C. S. Fenske, J. W. Garvin, J. J. Willaman, Q. Jones, B. G. Schubert, and H. S. Gentry, *J. Am. Pharm. Assoc.*, 48, 695 (1959) and earlier references there cited. (b) During the preparation of the present manuscript we were informed by Dr. Wall that recently he and his collaborators have also investigated *D. chiapasensis* and that they have isolated chiapagenin. Their structural conclusions coincide with ours.

(6) We are indebted to Dr. D. K. Cox of the Botanical Research Department, Syntex, S.A., Mexico, D. F. for this information and for a supply of the crude sapogenins.

(7) H. A. Walens, S. Serota, and M. E. Wall, *J. Org. Chem.*, 22, 182 (1957).

(8) M. E. Wall, C. R. Eddy, M. L. McClennan, and M. E. Klumpp, *Anal. Chem.*, 24, 1337 (1952); R. N. Jones, E. Katzenellenbogen, and K. Dobriner, *J. Am. Chem. Soc.*, 75, 158 (1953); A. L. Hayden, P. B. Smeltzer, and I. Scheer, *J. Am. Chem. Soc.*, 26, 550 (1954).

(9) C. Djerassi and R. Ehrlich, *J. Org. Chem.*, 19, 1351 (1954).

(10) C. Sannié and H. Lapin, *Bull. Soc. Chim. France*, 1237 (1957). The physical constants of neoruscogenin and its diacetate are quite different from those of chiapagenin and IVb.

remaining possibilities could be differentiated readily by infrared spectroscopy[11] and rotatory dispersion measurements.[12]

Selective acetylation of the homoallylic 3β-hydroxyl group was effected at room temperature and the resulting chiapagenin 3-monoacetate (IVc) was oxidized with chromium trioxide to afford in good yield correlogenin (I) acetate. This established the location of the unknown hydroxyl group at C-12, the only remaining uncertainty being its configuration. To settle this point, sisalagenin (VII)[13] was reduced with sodium borohydride to the corresponding diol (VIa), the equatorial β-orientation being assigned to the predominant isomer,[14] which was further characterized as the 3,12-diacetate (VIb) and the 12-monoacetate (VIc). The same substances were also obtained upon catalytic hydrogenation of chiapagenin diacetate (IVb) followed by partial or complete saponification, thus defining chiapagenin rigorously as 12β-hydroxyyamogenin (IVa).

EXPERIMENTAL[15]

Isolation of sapogenins. The collection of *Dioscorea chiapasensis* Matuda was carried out by Dr. D. K. Cox on the road between Santiago Atitlan and Chicacao, Suchitepequez (Guatemala). The dried and powdered roots (1 kg.) were heated under reflux for 2 hr. with 10 l. of denatured alcohol, the solvent was filtered, and the extraction repeated twice with fresh solvent. The combined extracts were concentrated to a volume of 5 l., 1.5 l. of concd. hydrochloric acid was added, and the mixture was heated under reflux for 4 hr. After diluting with 30 l. of ice water, the precipitate was filtered, washed with water, and finally dried *in vacuo* at 80° yielding 52 g. of crude material.

A suspension of 25 g. of crude sapogenins and 4.0 g. of Girard's reagent T in 150 cc. of absolute ethanol and 15 cc. of acetic acid was heated under reflux for 1 hr. The cooled solution was added to an excess of saturated sodium bicarbonate solution and unchanged sapogenins were removed by three successive extractions with ether. The aqueous layer was acidified to *p*H 1 with concd. hydrochloric acid and then heated on the steam bath for 1 hr. Extraction with ether and chromatography of the residue after evaporation of the ether on 60 g. of alumina (activity III) afforded a semisolid in the benzene eluates. After one crystallization from aqueous alcohol followed by acetylation and recrystallization from ether hexane, there was isolated 13 mg. of *correlogenin* (neobotogenin) (I) *acetate*,[7] m.p. 211–212° Identity was established by mixture melting point determination and infrared comparison with an authentic sample of the acetate of correlogenin, isolated from *Dioscorea spiculiflora* Hemsl and which was kindly supplied by Dr. A. Bowers of Syntex, S.A., Mexico, D. F.

A portion (8.8 g.) of the nonketonic sapogenins (23.5 g.) was chromatographed on 350 g. of alumina (activity III) with the following results. Elution with 500 cc. of benzene afforded, after crystallization from ethanol, 0.46 g. of a colorless substance m.p. 194–195°, $[\alpha]_D$ −188° (*c*, 1.1), whose ultraviolet absorption maxima at 227, 235, and 242 mμ indicated that it was the $\Delta^{3,5}$-diene of chiapagenin produced by dehydration[16] during the acid hydrolysis and it was not further investigated.

Anal. Calcd. for $C_{27}H_{40}O_3$: C, 78.59; H, 9.77. Found: C, 78.70; H, 9.81.

Further elution with benzene-ether (8:2) gave 1.78 g. of crystals, m.p. 180–187°, which were found to be a difficultly separable mixture of *yamogenin* (II) and *diosgenin* (III). Chromatography of 2.1 g. of the acetylated mixture on 80 g. of alumina (activity II) provided 110 mg. of impure diosgenin acetate (m.p. 179–184°) as the first fraction eluted by hexane-benzene (1:1) and 370 mg. of impure yamogenin acetate (m.p. 174–176°) as the last fraction. Rechromatography and crystallization of the crude diosgenin acetate gave 21 mg. of the pure substance, m.p. 196–197°, $[\alpha]_D$ −126°, whose identity was established by mixture melting and infrared comparison with an authentic sample.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.27; H, 9.71; O, 14.02. Found: C, 76.11; H, 9.95; O, 14.18.

Recrystallization of the crude yamogenin acetate from ethanol led to 219 mg. of the pure product, m.p. 177–178°, $[\alpha]_D$ −126°.

Anal. Found: C, 76.34; H, 9.69; O, 14.05.

Hydrolysis gave yamogenin, m.p. 195–196°, undepressed upon admixture with a sample kindly furnished by Dr. M. E. Wall, U.S.D.A. Plant Products Laboratory (Philadelphia, Pa.). The infrared spectra of the two specimens in carbon disulfide solution were identical.

When the column was washed with benzene-ether (6:4), there was obtained 4.03 g. of solid, which after one recrystallization from ethanol led to 3.8 g. of crude *chiapagenin* (IVa), m.p. 240–245°. The *diacetate* (IVb) was prepared by heating under reflux for 1 hr. a sample of the sapogenin with acetic anhydride and recrystallizing from ethanol, m.p. 194–196°, $[\alpha]_D$ −128° (*c*, 1.9).

Anal. Calcd. for $C_{31}H_{46}O_5$: C, 72.34; H, 9.01; O, 18.65. Found: C, 72.51; H, 9.09; O, 18.40.

Pure chiapagenin (IVa) was regenerated from the acetate and recrystallized from ethanol, m.p. 257–259°, $[\alpha]_D$ −130° (*c*, 1.2). The infrared spectrum in carbon disulfide solution had a strong band at 922 cm.$^{-1}$ and a weak one at 895 cm.$^{-1}$ as well as one at 853 cm.$^{-1}$ indicative[8] of the "neo" (*e.g.*, II) rather than "iso" (*e.g.*, III) side chain configuration.

Anal. Calcd. for $C_{27}H_{42}O$: C, 75.28; H, 9.83; O, 14.88. Found: C, 74.96; H, 9.68; C, 15.47.

Oppenauer oxidation of chiapagenin. The oxidation was performed in the customary manner[17] by distilling some solvent from a mixture of 450 mg. of chiapagenin (IVa) and 3.1 cc. of cyclohexanone in 20 cc. of toluene, followed by the addition of 315 mg. of aluminum isopropoxide in 2 cc. of toluene and gentle refluxing for 4 hr. Water was added and the product was extracted with ether and dried. The ketone (V) crystallized from hexane-benzene as needles (190 mg.), m.p. 200–210°. The analytical sample was obtained from the same solvent pair and exhibited, m.p. 214–217°, $[\alpha]_D$ −13° (*c*, 1.0), $\lambda_{max}^{C_2H_5OH}$ 240 mμ, ε 16,800.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.66; H, 9.41; O, 14.93. Found: C, 75.12; H, 9.16; O, 15.36.

Conversion of chiapagenin (IVa) *to correlogenin* (I). Chiapagenin (IVa) (480 mg.) was acetylated with acetic anhydride (4 cc.) and pyridine (25 cc.) for 2 hr. at room temperature, and the product was extracted in the usual way. The crude monoacetate was dissolved in 5 cc. of ether

(11) R. N. Jones and F. Herling, *J. Org. Chem.*, 19, 1252 (1954).

(12) C. Djerassi and R. Ehrlich, *J. Am. Chem. Soc.*, 78, 440 (1956).

(13) R. K. Callow and V. H. T. James, *J. Chem. Soc.*, 1671 (1955). We are grateful to Dr. R. K. Callow of the National Institute for Medical Research, London, for a gift of sisalagenin.

(14) For similar reaction in the hecogenin series, see W. J. Adams, D. N. Kirk, D. K. Patel, V. Petrow, and I. A. Stuart-Webb, *J. Chem. Soc.*, 870 (1955).

(15) All melting points are corrected and were determined in capillaries inserted into the bath about 10° below the melting point. Rotations were determined in chloroform and ultraviolet absorption spectra in 95% ethanol.

(16) See W. J. Peal, *Chem. & Ind.* (*London*) 1451 (1957).

(17) C. Djerassi, *Org. Reactions*, 207–72 (1951).

and unchanged chiapagenin (140 mg.) was filtered. Chromatography of the ether-soluble fraction on 20 g. of alumina (activity I), elution with benzene-ether (8:2), and recrystallization from aqueous methanol yielded 325 mg. of chiapagenin 3-monoacetate (IVc), m.p. 176–177°, $[\alpha]_D$ −119° (*c*, 0.4).

Anal. Calcd. for $C_{29}H_{44}O_5$: C, 73.68; H, 9.38; O, 16.94. Found: C, 73.77; H, 9.18; O, 17.20.

To a solution of the monoacetate (IVc) (213 mg.) in 10 cc. of acetic acid was added at 10° a solution of 53 mg. of chromium trioxide in 25 cc. of acetic acid. After 30 min., water and ether were added, the organic phase was washed with water, then sodium bicarbonate, again with water, dried, and evaporated. Crystallization of the residue from aqueous methanol provided 151 mg. of correlogenin (I) acetate, m.p. 210–212°, undepressed upon admixture with an authentic sample, $[\alpha]_D$ −73° (*c*, 0.6). Identity was confirmed by infrared comparison.

Anal. Calcd. for $C_{29}H_{42}O_5$: C, 74.01; H, 9.00; O, 17.00. Found: C, 73.96; H, 8.97; O, 17.10.

Dihydrochiapagenin (VI). (a) *From chiapagenin* (IVa). Chiapagenin diacetate (IVb) (2.17 g.) was hydrogenated at atmospheric pressure in 50 cc. of acetic acid in the presence of 100 mg. of platinum oxide catalyst. The reaction was stopped after 2 hr. when 1.05 equivalents of hydrogen had been consumed. Chromatography of the reduction product on 100 g. of alumina and crystallization from methanol led to *dihydrochiapagenin diacetate* (VIb), m.p. 204–205°, $[\alpha]_D$ −76° (*c*, 0.6), while saponification with boiling 5% methanolic potassium hydroxide afforded *dihydrochiapagenin* (VIa), m.p. 202–204° (from aqueous methanol), $[\alpha]_D$ −79° (*c*, 1.1). Both substances were shown to be identical by mixture melting point determination and infrared comparison with the corresponding specimens prepared from sisalagenin [see (b) below].

Dihydrochiapagenin 12-monoacetate (VIc) was formed when 33 mg. of the diacetate (VIb) and 11.5 mg. of lithium hydroxide monohydrate[18] in 40 cc. of 80% ethanol was kept at 21° for 22 hr. The solution was diluted with water, extracted with ether, and the product was crystallized from hexane-benzene, m.p. 213–214°, $[\alpha]_D$ −84° (*c*, 0.3).

Anal. Calcd. for $C_{29}H_{46}O_5$: C, 73.37; H, 9.77; O, 16.86. Found: C, 73.57; H, 9.92; O, 16.59.

(b) *From sisalagenin* (VII). Sodium borohydride (13 mg.) was added to a solution of 109 mg. of sisalagenin (VII) acetate[12] in absolute ethanol, and the mixture was heated under reflux for 2 hr. Sodium hydroxide (100 mg.) was then added and heating continued for a further 1 hr. After dilution with water, the product (VIa) was extracted with ether and crystallized from aqueous methanol, m.p. 204–205°, $[\alpha]_D$ −73° (*c*, 0.7). A polymorphic form with m.p. 194–196° was also encountered.

Anal. Calcd. for $C_{27}H_{44}O_4.CH_3OH$: C, 72.37; H, 10.41; O, 17.22. Found: C, 72.58; H, 10.32; O, 16.72.

Acetylation followed by recrystallization from methanol gave the diacetate VIb, m.p. 204–205°

Anal. Calcd. for $C_{31}H_{46}O_6$: C, 72.06; H, 9.36. Found: C, 72.07; H, 9.37.

Selective saponification of the diacetate (VIb) with lithium hydroxide as described under (a) yielded the 12-monoacetate (VIc), m.p. 213–214°, $[\alpha]_D$ −80° (*c*, 0.7), which proved to be identical in all respects with the corresponding specimen derived from chiapagenin.

Addendum (June 28, 1960): A new and larger batch of *Dioscorea chiapasensis* was worked up recently and in addition to chiapagenin (IVa), yamogenin (II), and diosgenin (III) there was isolated a new sapogenin, which proved to be isochiapagenin (12β-hydroxydiosgenin). Its structure was established by monoacetylation at C-3 followed by oxidation to botogenin acetate[7] (12-ketodiosgenin acetate) as well as by partial synthesis involving sodium borohydride reduction of botogenin acetate.

EXPERIMENTAL

A 7-kg. lot of *D. chiapasensis* was worked up as above to yield 67 g. of crystalline and 63 g. of oily sapogenin mixture. Chromatography of the crystalline fraction afforded 13 g. of diosgenin mixed with yamogenin and 22 g. of chiapagenin. Similar chromatography of the oily material (63 g.) produced 20 g. of crude $\Delta^{3,5}$-diene, 14 g. of diosgenin-yamogenin mixture and (after acetylation) 0.535 g. of *isochiapagenin (12β-hydroxydiosgenin) 3,12-diacetate*, m.p. 206–207° (recrystallized from hexane), $[\alpha]_D$ −120° (*c*, 1.3).

Anal. Calcd. for $C_{31}H_{46}O_6$: C, 72.34; H, 9.01; O, 18.65. Found: C, 72.11; H, 9.11; O, 19.15.

Saponification with boiling 5% ethanolic sodium hydroxide solution and recrystallization from methanol provided *isochiapagenin*, m.p. 236–237°, $[\alpha]_D^{23}$ −121° (*c*, 0.8).

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83; O, 14.86. Found: C, 74.95; H, 10.25; O, 14.79.

Monoacetylation of 101 mg. of isochiapagenin as described above for chiapagenin and recrystallization from hexane led to 60 mg. of the 3-monoacetate, m.p. 208–210°.

Anal. Calcd. for $C_{29}H_{44}O_5$: C, 73.68; H, 9.38; O, 16.94. Found: C, 73.44; H, 9.27; O, 17.17.

Oxidation of 50 mg. of the monoacetate with 15 mg. of chromium trioxide afforded 31 mg. of botogenin acetate,[7] m.p. 226–227°, $[\alpha]_D$ −56° (*c*, 0.8), whose identity was established by mixture melting point determination and infrared comparison with an authentic sample.

Anal. Calcd. for $C_{29}H_{42}O_5$: C, 74.01; H, 9.00. Found: C, 73.75; H, 8.71.

Reduction of 97 mg. of botogenin acetate in 10 cc. of absolute ethanol with 13 mg. of sodium borohydride (2 hr. refluxing) followed by acetylation and one recrystallization from methanol gave isochiapagenin acetate, m.p. 206–207°, identical in all respects with a specimen derived from the naturally occurring material.

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(18) R. Hirschmann, C. S. Snoddy, C. F. Hiskey, and N. L. Wendler, *J. Am. Chem. Soc.*, **76**, 4013 (1954).