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Steroids and Related Natural Products. VII. Boron Trifluoride Etherate–Lithium Aluminum Hydride Reduction of Smilagenin Acetate[1,2]

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Reduction of smilagenin acetate (Va) using a boron trifluoride etherate-lithium aluminum hydride reagent, followed by hydrogen peroxide oxidation and acetylation, was found to yield: 3β-ethoxysmilagenin (Vb), 3β-ethoxydihydrosmilagenin acetate (VIa), dihydrosmilagenin diacetate (VIb), and a complex mixture of partially acetylated products. Similar reaction conditions were employed to convert dihydrodiosgenin (II) to dihydrochlorogenin (III). Boron trifluoride etherate-lithium aluminum hydride reduction of 3β-acetoxy-5α-cholestane and 3β-acetoxy-5α-lanostane (VIIIa) was shown to yield the corresponding 3β-ethoxy (*e.g.*, VIIIb) derivatives.

The steroidal sapogenin spiroketal system is essentially inert to attack by lithium aluminum hydride in ether solution. However, a reagent prepared from aluminum chloride and lithium aluminum hydride readily reduces a steroidal sapogenin to its corresponding dihydro derivative (*e.g.*, I → II).[4] Previous experience with a reaction involving steroidal sapogenins and ethanedithiol in boron trifluoride etherate[5] suggested that a boron trifluoride–catalyzed lithium aluminum hydride reduction sequence might also provide a route to dihydrosapogenins.[6] Consequently, in 1958 during a study concerned with the preparation of dihydrosapogenins,[4] diosgenin acetate (I) was dissolved in boron trifluoride etherate and added to a cooled suspension of lithium aluminum hydride. The ensuing reaction produced a complex mixture of boron-containing products. When the first reported examples[7] of olefin hydroboration by aluminum chloride–sodium borohydride mixtures came to our attention, it appeared likely that the Δ^5 system of diosgenin had complicated the course of reduction. This side reaction was adequately illustrated in a subsequent experiment. When dihydrodiosgenin (II)[4] was subjected to the modified reaction and isolation procedure noted in the sequel, the product was dihydrochlorogenin (III). Aluminum chloride–lithium aluminum hydride reduction[4] of chlorogenin diacetate (IV → III) was used to verify the structure assignment.

Smilagenin acetate (Va) was selected for further studies in order to remove any obvious possibility of concomitant reaction(s) involving the steroid nucleus. It was also considered desirable to incorporate a hydrogen peroxide oxidation step to eliminate any boron-containing side products.[7] Surprisingly, reduction of smilagenin acetate with a boron trifluoride etherate–lithium aluminum hydride reagent yielded a number of products. Therefore, the crude mixture was acetylated and carefully chromatographed. Initial chromatographic separation on activated alumina led to isolation of 3β-ethoxysmilagenin (Vb), 3β-ethoxydihydrosmilagenin acetate (VIa) and dihydrosmilagenin diacetate (VIb). Structures for these compounds were tentatively assigned following an inspection of their infrared spectra and elemental compositions. A substantial portion of the remaining complex mixture obtained by boron trifluoride–catalyzed reduction of smilagenin acetate appeared to contain an unacetylated alcohol (ν_{max}^{KBr} 3330 cm.$^{-1}$).

Conclusive evidence for the formation of 3β-ethoxysmilagenin was provided by ethylation of smilagenin (Vc) with ethyl iodide in the presence of silver oxide. The authentic 3β-ether (Vb) was identical with the reduction product. Ethylation of smilagenin was actually first attempted by heating its potassium derivative in toluene with ethyl iodide. After acetylating the crude product, only epismilagenin acetate (VIIa) was isolated.[8,9] Ethylation of epismilagenin (VIIb) was also achieved using the ethyl iodide–silver oxide pro-

(1) Part VI, G. R. Pettit, B. Green, and W. J. Bowyer, *J. Org. Chem.*, **26**, 4773 (1961).

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(4) G. R. Pettit and W. J. Bowyer, *J. Org. Chem.*, **25**, 84 (1960). Leading references to several useful catalytic hydrogenation procedures, for converting steroidal sapogenins to their dihydro derivatives, are also cited in this paper.

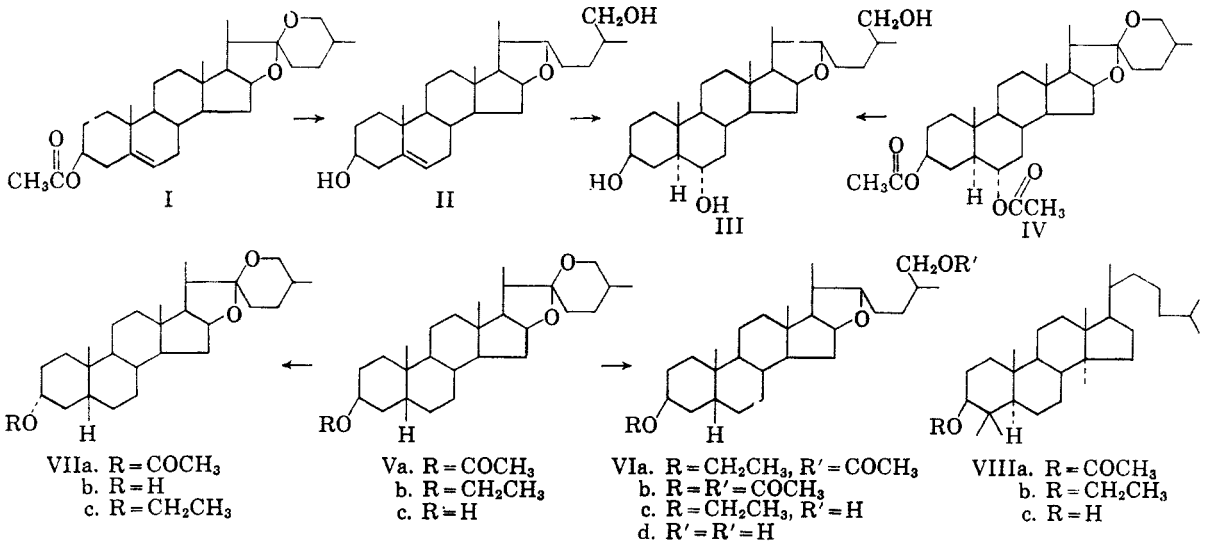
(5) C. Djerassi, O. Halpern, G. R. Pettit, and G. H. Thomas, *J. Org. Chem.*, **24**, 1 (1959).

(6) See, ref. 4, footnote 10.

(7) For example see, H. C. Brown, and B. C. Subba Rao, *J. Am. Chem. Soc.*, **78**, 5694 (1956). Leading references to the Brown hydroboration reaction may be obtained by consulting a recent report by H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 487 (1961).

(8) Inversion of the axial 3β-hydroxy group of smilagenin to the more stable 3α-configuration, under these conditions, was not considered unusual. Although J. R. Lewis and C. W. Shoppee, *J. Chem. Soc.*, 1375 (1955), have reported several analogous examples where ether formation proceeded with retention of configuration, partial epimerization was observed with a prolonged reaction time.

(9) Syntheses of epismilagenin (by lithium aluminum hydride reduction of smilagenone) and its acetate derivative have been described by C. Djerassi, R. Yashin, and G. Rosenkranz, *J. Am. Chem. Soc.*, **74**, 422 (1952).



cedure. The 3β-configuration of the smilagenin acetate reduction product Vb received support from an infrared spectral comparison with the authentic sample of 3α-ethoxysmilagenin (VIIc). Differences observed in the fingerprint region were consistent with epimeric structures. These experiments also served to illustrate the stereospecific nature of the novel reduction reaction which led to 3β-ethoxysmilagenin.[10]

Additional support for the 3β-ethoxysmilagenin structural assignment was obtained as a result of the following experiments. Boron trifluoride etherate–lithium aluminum hydride reduction of both 3β-acetoxy-5α-cholestane and 3β-acetoxy-5α-lanostane (VIIIa) yielded 3β-ethoxy derivatives (*e.g.*, VIIIb).[10a] The structure of each product was established by ethylation (ethyl iodide–potassium or silver oxide) of the corresponding alcohols. Both procedures led to rather low yields of the 3β-ethoxy compounds.

Authentic specimens of 3β-ethoxydihydrosmilagenin and dihydrosmilagenin were obtained by aluminum chloride–lithium aluminum hydride reduction[4] of 3β-ethoxysmilagenin and smilagenin acetate respectively. The acetate derivative of each substance proved to be identical with its corresponding component isolated from the smilagenin acetate reduction products.

In order to eliminate any apparent opportunity for ether formation, the reduction reaction was next investigated using smilagenin. Boron trifluoride etherate–lithium aluminum hydride reduction of smilagenin was followed by hydrogen peroxide oxidation and acetylation of the crude product. In this case, chromatographic separation led to isolation of smilagenin acetate, dihydrosmilagenin diacetate, and a glass-like mixture of partially acetylated products.[11–13] The complex mixture of products obtained using the lithium aluminum hydride–boron trifluoride etherate reagent precludes the use of this procedure as a preparative route to dihydrosmilagenin.

EXPERIMENTAL[14]

Chromatography. Acid-washed and activated alumina refer to Merck aluminum oxide, "acid washed" and "suitable for chromatography" respectively. The chromatographic separations were performed using an alumina to organic mixture ratio of 30:1 by weight. Petroleum ether refers to the fraction boiling at 40–60°.

Acetylation. Preparation of acetate derivatives was accomplished in each case using 1:1 acetic anhydride–pyridine (steam bath, 1 hr.). Following removal of solvent (*in vacuo*) the residue was dissolved in ether and washed successively with 2*N* hydrochloric acid, 1*N* sodium hydroxide and water.

(10) The potentialities of this new reaction led us to investigate its usefulness as a method for synthesis of certain other ethers and oxygen heterocyclic compounds. Several aspects of this study have been summarized in preliminary communications prepared by: (a) G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, **25**, 875 (1960); (b) G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, **26**, 986 (1961); (c) G. R. Pettit, U. R. Ghatak, B. Green, T. R. Kasturi, and D. Piatak, *J. Org. Chem.*, **26**, 1685 (1961); and (d) see ref. 1. The mechanism of this ester → ether reduction reaction has been discussed in part VIII of this series: *cf.*, G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, **26**, 4557(1961).

(11) It was evident that dihydrosmilagenin was not an important intermediate in the production of these compounds as *ca.* 80% of starting material was recovered when dihydrosmilagenin was subjected to the reduction reaction sequence.

(12) Recently, a one-step procedure for oxidation of diosgenin to 3β,5α,6β,16β,20α-pentahydroxypregnane using hydrogen peroxide or one of several other oxidizing agents has been claimed by H. Nawa, A. Nishikawa, and M. Nishikawa, U. S. Patent **2,966,502**, Dec. 27, 1960. However, smilagenin acetate was unaffected by the mild hydrogen peroxide oxidation conditions used in the present study.

(13) The structures of these substances are presently under investigation.

(14) Melting points are uncorrected and were observed using open Kimble glass capillaries in a silicone oil bath. Microanalyses were provided by Dr. A. Bernhardt, Mülheim, Germany. The optical rotation (chloroform solution) measurements were carried out in the laboratory of Drs. Weiler and Strauss, Oxford, England. Dr. R. A. Hill, of this laboratory, recorded the infrared spectra.

Saponification. This reaction was carried out using a 1*N* solution of potassium hydroxide in methanol. After heating (steam bath) for 1 hr. and dilution with water, the product was isolated.

Boron trifluoride etherate–lithium aluminum hydride reduction of smilagenin acetate (Va). A solution of smilagenin acetate (2.43 g.) in 325 ml. of dry ether containing boron trifluoride etherate (26 ml.) was added over a 15-min. period to a cooled (ice bath) suspension of lithium aluminum hydride (2.0 g.) in dry ether (225 ml.). Stirring and cooling were continued for a 45-min. period before heating the mixture at reflux for 2 hr. The reaction mixture was again cooled and cautiously treated with dilute hydrochloric acid. The ether layer was separated and washed successively with 1*N* hydrochloric acid, 1*N* sodium bicarbonate and water. Removal of solvent from the ether solution provided a residue which was dissolved in warm (70°) ethanol (30 ml.) containing sodium hydroxide (0.5 g.). Following addition of 30% hydrogen peroxide (5 ml.), the solution was heated for 5 min. Dilution with water precipitated a solid which was collected, dried and acetylated. The crude acetylation product was chromatographed on activated alumina and elution with 3:1 petroleum ether–benzene gave 0.23 g. of crystalline product melting at 152–154°. Elimination of the hydrogen peroxide oxidation step, in a prior experiment, led to approximately the same yield of this substance (Vb). Recrystallization from methylene chloride–methanol afforded a pure sample of *3β-ethoxysmilagenin* (Vb)[15] as colorless plates; m.p. 153–154°, $[\alpha]_D^{23}$ −48.9°, $\nu_{max}^{CHCl_3}$ 1100 cm.$^{-1}$

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.37; H, 10.81. Found: C, 78.08; H, 10.99.

Elution with benzene yielded 0.5 g. of *3β-ethoxydihydrosmilagenin acetate* (VIa) which recrystallized from methanol as colorless needles; m.p. 80–81°, $[\alpha]_D^{22}$ 0.0°.

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.17; H, 10.72; O, 13.10. Found: C, 76.21; H, 10.63; O, 13.07.

Further elution employing benzene-ether (3:1) yielded 0.32 g. of crystalline product. Two recrystallizations from methanol led to a pure specimen of *dihydrosmilagenin diacetate* (VIb), m.p. 90–92°.[16]

Ether containing a trace of methanol was used to elute the remaining mixture of products (1.5 g.).

The structures assigned to each of the above products were confirmed by mixture melting point determination and infrared spectral comparison with their respective authentic samples (described in the sequel).

Attempted ethylation of smilagenin (Vc). A stirred solution of smilagenin (1.56 g.)[17] in 50 ml. of anhydrous toluene containing potassium sand (0.15 g.), in suspension, was heated at reflux for 2 hr. The mixture was then cooled and treated with ethyl iodide (4.5 g.). After a 4-hr. period at reflux, the mixture was poured into water. The separated toluene solution was washed with water and dried (sodium sulfate). The residue obtained following removal of solvent was acetylated and chromatographed on activated alumina. Elution with petroleum ether–benzene (1:1) gave 1.03 g. of 3α-acetoxysmilagenin (VIIa),[9] m.p. 162–164°. Two recrystallizations from acetone yielded a pure sample as colorless needles melting at 163–164°, $[\alpha]_D^{22}$ − 40.5°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.91; H, 10.11; O, 13.95. Found: C, 76.31; H, 10.11; O, 13.83.

3α-Ethoxysmilagenin (VIIc). Freshly prepared silver oxide (1.25 g.) was added during 90 min. to a mixture composed of Drierite (1.3 g.)[18] and a refluxing solution of epismilagenin (VIIb, 0.67 g.)[19] in ethyl iodide (15 ml.). Two hours after adding the oxide, the mixture was cooled and filtered. The residue obtained by concentrating the filtrate to dryness was chromatographed on acid-washed alumina. Elution with 3:1 petroleum ether–benzene yielded 0.45 g., m.p. 148–152°, of 3α-ethoxysmilagenin. Three recrystallizations from acetone gave an analytical sample as colorless needles; m.p. 161–162°, $[\alpha]_D^{23}$ −39.9°, $\nu_{max}^{CHCl_3}$ 1100 cm.$^{-1}$

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.37; H, 10.81; O, 10.82. Found: C, 78.08; H, 10.81; O, 10.72.

3β-Ethoxysmilagenin (Vb). Ethylation of smilagenin (Vc, 1.0 g.)[17] with ethyl iodide (15 ml.) in the presence of silver oxide (1.5 g.) and Drierite (1.5 g.) was accomplished as described in the preceding experiment. The crude product was chromatographed on acid-washed alumina. Petroleum ether–benzene (3:1) eluted 0.65 g. of solid product (Vb) which recrystallized as colorless needles from acetone, m.p. 153–155°.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.37; H, 10.81; O, 10.82. Found: C, 77.79; H, 10.65; O, 11.12.

3β-Ethoxydihydrosmilagenin acetate (VIa). Reduction of 3β-ethoxysmilagenin (0.45 g.) to the dihydro derivative VIc was achieved using lithium aluminum hydride (0.38 g.)–aluminum chloride (5.7 g.) in ether solution (75 ml.).[20] The crude product was acetylated and chromatographed on activated alumina. Elution with benzene yielded 0.31 g. of semisolid material (VIa). Two recrystallizations from methanol gave colorless needles, m.p. 81–82°.

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.17; H, 10.72; O, 13.10. Found: C, 76.02; H, 10.63; O, 13.07.

The acetate was saponified and the crude product, m.p. 95–98°, recrystallized from methanol. A pure sample of *3β-ethoxydihydrosmilagenin* (VIc) was obtained as colorless flakes; m.p. 104–106°, $[\alpha]_D^{22}$ + 9.9°.

Anal. Calcd. for $C_{29}H_{50}O_3$: C, 77.97; H, 11.29; O, 10.73. Found: C, 77.93; H, 11.18; O, 10.74.

Dihydrosmilagenin diacetate. (VIb). Smilagenin acetate (Va, 2.0 g.) was reduced in ether (400 ml.) solution employing the aluminum chloride (26 g.)–lithium aluminum hydride (1.8 g.) reagent.[20] The crude product weighed 1.8 g. One recrystallization from benzene gave colorless needles melting at 149–153°. Repeated recrystallization from ethyl acetate yielded a pure sample (1.5 g.), m.p. 161–163°, of *dihydrosmilagenin* (VId).[16] Treating the diol (VId) with acetic anhydride-pyridine and recrystallizing the resulting acetate from methanol led to a sample of dihydrosmilagenin diacetate melting at 91–92°.[16]

3β-Ethoxy-5α-cholestane. A. Reduction of 3β-acetoxy-5α-cholestane. A solution of 3β-acetoxy-5α-cholestane (1.1 g.) in dry ether (100 ml.) containing boron trifluoride etherate (12 ml.) was allowed to react with a mixture composed of lithium aluminum hydride (1.0 g.) and dry ether (100 ml.). This experiment was carried out as described for the reduction of smilagenin acetate. Hydrogen peroxide treatment proved to be unnecessary. Acetylation, followed by chromatography of the crude product on activated alumina, and elution with petroleum ether gave 3β-ethoxy-5α-cholestane (0.17 g.).[21] Recrystallization from methylene chloride-methanol afforded an analytical sample as colorless needles melting at 81–83°; $[\alpha]_D^{20}$ +23.8°, ν_{max}^{KBr} 1112 and 1129 cm.$^{-1}$

Anal. Calcd. for $C_{29}H_{52}O$: C, 83.53; H, 12.58; O, 3.89. Found: C, 83.47; H, 12.56; O, 3.91.

(15) A referee has suggested that a stereochemical change in rings E or F may be responsible for the low negative rotation recorded for ether Vb as compared to 3β-acetoxysmilagenin, $[\alpha]_D^{25}$ −69° (chloroform): see, M. E. Wall, M. M. Krider, E. S. Rothman, and C. R. Eddy, *J. Biol. Chem.*, **198**, 533 (1952).

(16) I. Scheer, R. B. Kostic, and E. Mosettig, *J. Am. Chem. Soc.*, **77**, 641 (1955).

(17) Smilagenin was prepared by saponification (*cf.*, ref. 16) or lithium aluminum hydride (ether solution) reduction of the corresponding acetate.

(18) *Cf.* H. G. Fletcher, Jr., and R. K. Ness, *J. Am. Chem. Soc.*, **77**, 5337 (1955).

(19) Prepared by saponification of 3α-acetoxysmilagenin.

(20) Consult the general procedure described in ref. 4.

(21) See also, C. Djerassi, M. Shamma, and T. Y. Kan, *J. Am. Chem. Soc.*, **80**, 4723 (1958).

The infrared spectrum (chloroform solution) of this substance was identical with that of the authentic sample described below; a mixture melting point was undepressed.

B. Ethylation of 3β-hydroxy-5α-cholestane. Ethyl iodide (5 g.) was used to ethylate 3β-hydroxy-5α-cholestane (1.9 g.) in toluene (5 ml.) solution containing suspended potassium sand (0.2 g.). The reaction was performed as described above for attempted ethylation of smilagenin. Chromatography on activated alumina and elution with petroleum ether yielded 0.22 g. of solid melting at 75–78°. A pure sample recrystallized from methylene chloride–methanol as fine needles, m.p. 82–84°.

3β-Ethoxy-5α-lanostane (VIIIb). *A. Reduction of 3β-acetoxy-5α-lanostane* (VIIIa). Boron trifluoride etherate-lithium aluminum hydride reduction of 3β-acetoxy-5α-lanostane (0.69 g.)[22] was accomplished as previously described for reduction of 3β-acetoxy-5α-cholestane. In this case, the fraction eluted with petroleum ether weighed 0.26 g. (38%) and melted at 130–132°. Two recrystallizations from methylene chloride–methanol yielded a pure specimen (VIIIb); colorless flakes, m.p. 134–135°, $[\alpha]_D^{20}$ +53.2°, $\nu_{max}^{CHCl_3}$ 1100 cm.$^{-1}$

Anal. Calcd. for $C_{33}H_{58}O$: C, 83.84; H, 12.66; O, 3.49. Found: C, 83.62; H, 12.47; O, 3.97.

Continued elution employing petroleum ether–benzene (3:1) yielded 3β-acetoxy-5α-lanostane (0.36 g.), m.p. 150–152°.

B. Ethylation of 3β-hydroxy-5α-lanostane (VIIIc). A stirred mixture of 3β-hydroxy-5α-lanostane (1.5 g.),[22] freshly prepared silver oxide (1.0 g.), ethyl iodide (5 ml.) and dimethylformamide (50 ml.) was heated at 60–70° for 10 hr.[23] Additional quantities of silver oxide (0.5 g.) and ethyl iodide (4 ml.) were added and heating was continued over a 12-hr. period. After dilution with chloroform, the red mixture was filtered and the filtrate washed with aqueous 5% potassium cyanide and water. Following removal of the dry (sodium sulfate) solvent, the residue was acetylated and chromatographed on activated alumina. Elution with petroleum ether yielded 0.13 g. of solid melting at 127–130°. Recrystallization from methylene chloride–methanol did not appreciably change the melting point (129–130°). However, mixture melting point determination and infrared spectral comparison (potassium bromide) with the substance (VIIIb) obtained in part A established identity of both products.

Elution with 3:1 petroleum ether–benzene was used to recover 0.65 g. of 3β-acetoxy-5α-lanostane melting at 151–152°.

Boron trifluoride etherate–lithium aluminum hydride reduction of smilagenin (Vc). The reaction involving smilagenin (8.32 g., in 600 ml. of ether), boron trifluoride etherate (94 ml.) and lithium aluminum hydride (6.0 g. in 600 ml. of ether) was carried out as described in the case of smilagenin acetate. Following treatment with hydrogen peroxide and acetic anhydride–pyridine, the oily product (9.0 g.) was chromatographed on activated alumina. Elution with benzene gave 1.45 g. of *smilagenin acetate*, m.p. 151–153°. Further elution with benzene-ether (5:1) yielded *dihydrosmilagenin diacetate* (0.54 g., m.p. 88–91°). The fractions (6.8 g. total) eluted with ether and ether-methanol were combined, reacetylated and rechromatographed on acid-washed alumina. Elution with benzene and 9:1 benzene-ether afforded 3.53 g. of dihydrosmilagenin diacetate, m.p. 88–90°. A small sample purified by recrystallization from methanol melted at 90–92°. This product (VIb) and recovered smilagenin acetate were identical (mixture melting point and infrared spectral comparison) with authentic specimens.

Continued elution with 1:3 benzene-ether yielded a viscous residue (2.83 g.) which resisted attempts to effect crystallization.[18]

Attempted reaction between dihydrosmilagenin (VId) *and boron trifluoride etherate–lithium aluminum hydride.* The previous experiment was repeated employing 0.75 g. of dihydrosmilagenin and proportionately adjusted quantities of reactants and solvents. Prior to acetylation the crude product melted at 161–164°. Recrystallization from ethyl acetate gave 0.52 g. of starting material, m.p. 162–164°. The mother liquors were concentrated to dryness, acetylated (0.23 g. yield), and chromatographed on activated alumina. Elution with benzene-ether (1:1) led to 0.10 g. of dihydrosmilagenin diacetate melting at 91–92°. An oil weighing 0.06 g. was recovered by elution with ether–methanol.

Dihydrochlorogenin (III). A. *From dihydrodiosgenin* (II). Hydroxylation of dihydrodiosgenin (0.75 g.)[4] was accomplished using the boron trifluoride etherate–lithium aluminum hydride procedure, followed by hydrogen peroxide oxidation, as described for reduction of smilagenin acetate. After acetylation, the crude product (0.89 g.) was chromatographed on activated alumina. Benzene-ether (1:1) eluted a viscous oil (0.71 g.). Rechromatography on a new column of activated alumina and elution with the above solvent mixture gave 0.50 g. of oily product. Saponification provided a colorless solid melting at 233–235°. Recrystallization from methanol gave dihydrochlorogenin as colorless needles, m.p. 234–236° (sintering from 230°), $[\alpha]_D^{21}$ + 16.8° (pyridine).

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 74.61; H, 10.67. Found: C, 74.42; H, 10.35.

B. From chlorogenin diacetate (IV). The aluminum chloride (11 g.)–lithium aluminum hydride (0.77 g.) procedure[4] was used to reduce chlorogenin diacetate (0.88 g.).[24] In this case, the crude product proved to be essentially insoluble in the reaction solvent (270 ml. of ether). Following dilution with hydrochloric acid and separation of the ether layer, the insoluble material was collected by filtration and washed with water. The dry solid was acetylated, chromatographed (0.70 g. yield), and finally saponified as described in section A. Repeated recrystallization of the crude alcohol (0.37 g.), m.p. 218–222°, from methanol-water gave colorless needles melting at 228–231° (sintering from 225°). Although the purity of this substance (III) was questionable on the basis of melting point, it appeared to be identical (mixture melting point determination and infrared spectral comparison) with the compound prepared in part A.

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(22) C. S. Barnes and A. Palmer, *Australian J. Chem.*, **10**, 334 (1957).

(23) *Cf.*, R. Kuhn, I. Löw, and H. Trischmann, *Chem. Ber.*, **90**, 203 (1957).

(24) We are indebted to Professor Carl Djerassi for providing this substance.