and hydrogen (45 p.s.i.). One mole of hydrogen was absorbed in 45 min. The catalyst was filtered, the solvent removed and the residue distilled to yield 25.4 g. (72%) of β-dihydroeucarvone which boiled 42.5–44° (0.1 mm.), $n_D^{24.5}$ 1.4741, d_4^{25} 0.9286, MR_D obsd., 46.26, $\lambda_{max}^{C_2H_5OH}$ 241 mμ (log ε, 3.85).

The semicarbazone of this ketone melted at 162–165° (lit.[16,18] m.p. 162–165° and 201–202°) after recrystallization from ethanol.

The 2,4-dinitrophenylhydrazone melted at 193–195° (lit.[18] m.p. 194–195°).

B. A mixture of bromo ketone VI (10 g., 0.043 mole) and 2,6-lutidine (9.6 g., 0.086) was refluxed for 10 hr. Dilute hydrochloric acid was added and then ether was used to extract the product. Fractionation of the residue remaining after evaporation of the ether, produced β-dihydroeucarvone, VII (1.8 g.), b.p. 44–46° (0.4 mm.) and recovered bromide, VI (6.0 g.), b.p. 66° (0.4 mm.). The infrared spectrum and other properties of the sample of VII obtained in this way were identical with those of the sample obtained in part A.

The addition of bromine in acetic acid to VII produced dibromide VIII, 6.2 g. (44%), m.p. 69–71° (lit.[19] m.p. 71–72°), infrared band (chloroform) at 5.85 μ (1709 cm.$^{-1}$), and a yellow oil which was distilled, b.p. 70–75°, $n_D^{26.5}$ 1.5030, d_4^{26} 1.284, infrared bands (film) at 6.00 and 6.13 μ, $\lambda_{max}^{C_2H_5OH}$ 238 μ (log ε, 3.48). These properties suggested that this substance was the unsaturated ketone resulting from loss of hydrogen bromide from dibromide VIII; however, it decomposed rather rapidly at room temperature and was not investigated further.

(19) O. Wallach, *Ann.*, **418**, 58 (1919).

2,7-Dibromo-2,6,6-trimethylcycloheptanone (IX). The bromination of ketone V by the procedure of Wallach[9] produced IX in 73% yield as white needles, m.p. 65–67°, infrared bands (chloroform) at 5.80 (1724 cm.$^{-1}$) and 5.88 μ (1700 cm.$^{-1}$), (reported, lit.,[9] m.p. 68°).

Eucarvone (I). A slurry of ketone VII (7.6 g., 0.05 mole), *N*-bromosuccinimide (8.9 g., 0.05 mole) and carbon tetrachloride (50 ml.) was heated at reflux temperature for 3 hr. The succinimide was filtered, the solution washed with sodium bicarbonate, and water, and dried. The solvent was removed *in vacuo* and the residue (8.8 g.) was mixed with dry 2,6-lutidine (10.8 g., 0.10 mole) and heated at 85–90° for 3 hr. The reaction mixture was processed as in the preparation of VII from bromide VI. The first fraction (1.3 g.) was identified as eucarvone, b.p. 42–44° (1 mm.), $n_D^{24.8}$ 1.5051, $\lambda_{max}^{C_2H_5OH}$ 303 mμ (log ε, 3.83). The infrared spectrum was identical with that of a sample of eucarvone prepared from carvone.[4,6] Also the 2,4-dinitrophenylhydrazone melted at 151–153° alone or when mixed with an authentic derivative.

The second fraction from this reaction was carvacrol, XI, (3.2 g.), b.p. 52–53° (1 mm.), $n_D^{24.8}$ 1.5196, $\lambda_{max}^{C_2H_5OH}$ 278 mμ (log ε, 3.28). The identity of this product was established by comparison with an authentic sample of carvacrol obtained from the palladium catalyzed isomerization[20] of carvone.

New Brunswick, N. J.

(20) R. P. Linstead, K. O. A. Michaelis, and S. L. S. Thomas, *J. Chem. Soc.*, 1139 (1940).

[Contribution from the Division of Chemical Research, G. D. Searle & Co.]

The Synthesis of Steroid Ring-E Pyrroles and Pyrrolidines

George P. Mueller and James Jiu

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The direct transformation of kryptogenin to pentacyclic heterocycles containing nitrogen in ring E has been achieved by the use of anhydrous ammonia and ammonium or amine salts of formic or acetic acids.

Ring closure of the 1,4-diketone system of sarsasapogenoic acid and 5,6-dihydrokryptogenin, by hydrogenation of the dioximes, to form steroid pyrrolidines analogous to the dihydrosapogenins was first reported by Uhle and Jacobs.[1] Uhle and Sallmann[2] recently published an alternate method, involving zinc and acetic-acid reduction of kryptogenin 16-phenylhydrazones, affording the pyrrolidine as well as an interesting pyrroline intermediate. We wish to direct attention to our earlier experiments in this field[3] which were apparently overlooked in the latter publication. Our methods permit preparation of either the pyrrole or the pyrrolidine and we offer them as useful adjuncts to the synthesis of 16,22-iminocholestane derivatives.

By the Leuckart reaction[4] kryptogenin was converted to 3β,26-dihydroxy-16β,22-imino-5-cholestene, II. The latter and its *O,O,N*-triacetyl derivative appear to be identical with the same structures lately reported[2]; we also prepared a crystalline hydrochloride. The melting point of our Leuckart product V agrees fairly well with the 3β,27-dihydroxy-16β,22-methylimino-5-cholestene of Uhle and Sallmann, who reported no optical rotation value, however.

These authors suggested an α-configuration for the C_{-22} hydrogen atom, relative to the projected plane of the molecule, by virtue of catalytic and borohydride reduction of their pyrroline to the pyrrolidine through "attack from the rear."[5] To this we would add the hypothesis that chemical reduction by Leuckart conditions, leading from I to II and to V, would also take place through rear side attack, giving rise to pyrrolidines possessing C_{-16} and C_{-22} hydrogens α-oriented with respect to the

(1) F. C. Uhle and W. A. Jacobs, *J. Biol. Chem.*, **160**, 243 (1945).

(2) F. C. Uhle and F. Sallmann, *J. Am. Chem. Soc.*, **82**, 1190 (1960).

(3) G. P. Mueller, U. S. Patent **2,740,781**; *Chem. Abstr.*, **50**, 10804a (1956).

(4) M. L. Moore, *Org. Reactions*, V, 301 (1949).

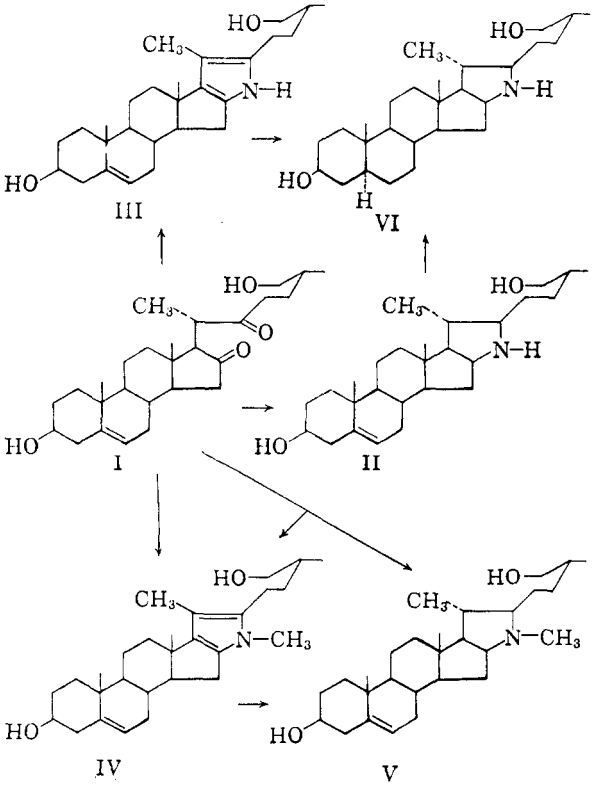
projected plane of the ring system. Indeed, although popularly written as 16β, the configuration of nitrogen in these molecules or even in solanidine has not been confirmed[6] except possibly by inference from "rear side" attack in the hydrogenation of sarsasapogenoic acid dioxime to the 16,22-imino compound, which was eventually converted into a known derivative of solanidine.[1]

Direct condensation of I with alcoholic ammonia afforded the pyrrole III, catalytic hydrogenation of which yielded 3β,26-dihydroxy-16β,22-iminocholestane, VI[7]; this was also obtained by hydrogenation of II. Such chemical evidence for the structure III[8] was reassuring in view of its curious spectral properties. The infrared absorption in chloroform showed prominant bands, 1719 cm.$^{-1}$ (m) and 1670 cm.$^{-1}$ (w), which were not exhibited by pyrrole itself or the compound IV. Moreover (see experimental) the strong absorption of III at 206 mμ was enhanced in hydrochloric acid with concomitant loss of a weak band at 236 mμ. More in character with a highly substituted pyrrole like cryptopyrrole,[9] compound IV displayed strong absorption at 206 mμ, somewhat diminished by hydrochloric acid which generated a new, strong band at 278 mμ.

An interesting sidelight on the Leuckart reaction was the reduction of the pyrrole IV to pyrrolidine V which was carried out under Leuckart conditions as a separate reaction. This isolation of a pyrrole intermediate, its reduction to the pyrrolidine and

(5) Although the configurational assignment of the C-22 hydrogen atom is clear from their structural formulas, Uhle and Sallmann have designated it as 22β. By the Fischer convention this is incorrect. In the terminology used (L. F. Fieser and M. Fieser, *Steroids*, Reinhold Publishing Corp., New York, N. Y., 1959, p. 337), 22α would be the correct designation. It should be noted that our nomenclature in this article is based on the usual α,β designations for the intact steroid nucleus, which we are extending to the five-ring nucleus of II.

Configurational nomenclature in the freely rotating steroid side chain is far from satisfactory. The Ciba Conference rules with the Plattner convention (L. F. Fieser and M. Fieser, Steroids, p. 338) represent the best device we have now. Unfortunately it does not lend itself to casual expression and is subject to errors, such as that above, which are most frequently due to a misunderstanding of the Fischer projection and its use. In fact this misunderstanding appears so frequently in texts and scientific papers that we wish to repeat Fischer's original description of his method (E. Fischer, *Ber.*, 24, 2684 (1891)): "Man construire zunächst mit Hülfe der so bequemen Friedlander'schen Gummimodelle die Moleküle der Rechtsweinsäure, Linksweinsäure und inactiven Weinsäuren und lege dieselben derart auf die Ebene des Papiers, dass die vier Kohlenstoffatome in einer geraden Linie sich befinden und dass die in Betracht Kommenden Wasserstoffe und Hydroxyle über der Ebene des Papiers stehen." Our translation: "To begin with, one may construct with the aid of the convenient Friedlander rubber models, the molecules of *d*-tartaric acid, *l*-tartaric acid, and inactive (*meso*)-tartaric acid. *They are then placed on the plane of the paper so that the four carbon atoms will lie on a straight line and the hydrogen atoms and hydroxyl groups in question will be oriented above the plane of the paper.*" The italics are ours.

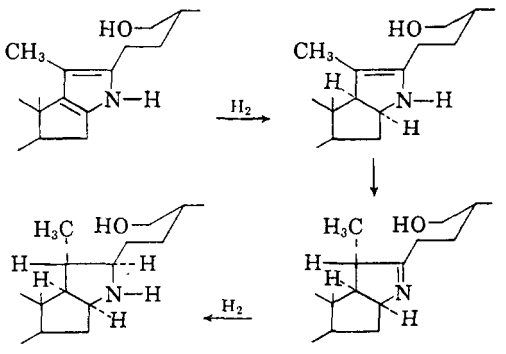


Further consideration of these matters has recently been published by L. F. Fieser and M. Fieser, *Tetrahedron*, 8, 360 (1960).

(6) V. Prelog and O. Jeger in *The Alkaloids*, vol. III, Academic, New York, 1953, p. 258; L. F. Fieser and M. Fieser in *Steroids*, Reinhold, New York, 1959, p. 848.

(7) Prepared and designated as 3β,27-dihydroxy-16β,22-iminocholestane by Uhle and Sallmann, *loc. cit.*

(8) Catalytic hydrogenation ordinarily would be expected to introduce an α-hydrogen at C-20, as it does with pseudosapogenins [M. E. Wall, C. R. Eddy, and S. Serota, *J. Am. Chem. Soc.*, **76**, 2849 (1954)]. If so, the C-20 epimer of VI would be obtained. That hydrogenation of II and III actually leads to the same product might be explained by conjugation of the hetero atom of III at the dihydropyrrole stage, leading, through various tautomeric forms, to a hydrogenation product having the natural C-20 α-methyl configuration. This idea is illustrated by the following mechanism:



Support for this scheme may be found in the stable 1-pyrroline structure proposed by Uhle and Sallmann and in the conditions for stability of natural and unnatural configurations at C-20 [N. Danieli, Y. Mazur, and F. Sondheimer, *Chem. and Ind.*, 1725 (1958); Y. Mazur and F. Sondheimer, *Experientia*, 16, 181 (1960).

(9) G. H. Cookson, *J. Chem. Soc.*, 2789 (1953).

the requirements of the stereochemistry at C_{-20} combine to indicate that the Leuckart reaction here proceeds from a pyrrole through a 1-pyrroline to the pyrrolidine. The last stage of reduction is equivalent to reduction of the imine intermediate proposed in the mechanism of the Leuckart reaction.[4]

One curious feature, noted under the preparation of II, was the isolation of yamogenin as one of the products. As both kryptogenin and yamogenin may be obtained from various species of *Dioscoreas*,[10] we considered that our kryptogenin might be impure. Attempts to separate yamogenin chromatographically were not definitive. Lacking evidence for the purity of our kryptogenin we have done no more than consider the intriguing possibility of yamogenin formation under the reaction conditions.

EXPERIMENTAL

Melting points were taken on the Kofler hot stage and are corrected. All rotations were measured at about 1% concentration in chloroform.

3β,26-Dihydroxy-16β,22-imino-5-cholestene (II). Eighty grams of formic acid was mixed carefully in the cold with 105 g. of concd. ammonia; 4.30 g. of kryptogenin was added and the solution distilled slowly under nitrogen. The temperature of the mixture was kept at 134–137° for 2 hr. during which the kryptogenin changed into a light tan oil with bubbling. The mixture was cooled and the solidified gum washed with water, dissolved in 70 ml. of alcohol and refluxed 3 hr. under nitrogen with 30 g. of potassium hydroxide in 20 ml. of water. Extraction with ether, washing, drying, and evaporation left 5.0 g. of a medium-brown glass. Chromatography on alumina yielded two fractions of interest. The first, eluted with 20% ether in benzene, appeared as 0.75 g. of plates, which for verification of identity were purified by chromatography again and recrystallized three times from methyl alcohol to yield yamogenin, m.p. 186–188°, $[\alpha]_D$ −132.5°, with which the analyses agreed.[11]

The second fraction of interest was eluted some while later with 40% ether in benzene and totaled 0.87 g. of needles, m.p. 175–176°, after two recrystallizations from ethyl acetate. An analytical sample, recrystallized twice more, m.p. 176.5–177.8°, $[\alpha]_D$ −29°, represented the pure imine II.

Anal. Calcd. for $C_{27}H_{45}NO_2$: C, 78.01; H, 10.91; N, 3.37. Found: C, 78.20; H, 10.71; N, 3.57.

The hydrochloride was prepared by treating 0.10 g. of imine in 50 ml. of methyl alcohol with 50 ml. of 1.2*N* hydrochloric acid, removing the alcohol *in vacuo* and collecting the fine precipitate. This was dissolved in 1 ml. of methyl alcohol and crystallized by careful addition of ether. The imine hydrochloride, crystallizing as micro needles, melted at 305–310°, $[\alpha]_D$ −10.4° (methanol).

Anal. Calcd. for $C_{27}H_{46}ClNO_2$: C, 71.72; H, 10.26; N, 3.10; Cl, 7.84. Found: C, 71.63; H, 10.00; N, 3.21; Cl, 8.05.

Acetylation by refluxing 0.10 g. of imine with 5 ml. of acetic anhydride for 30 min., followed by ether extraction, as is usual, led to an oil which crystallized slowly from a concentrated solution in pentane. Recrystallization from pentane yielded 3β,26-diacetoxy-16β,22-acetylimino-5-cholestene as irregular plates, m.p. 97–98°, $[\alpha]_D$ −37.6°.

Anal. Calcd. for $C_{33}H_{51}NO_5$: C, 73.16; H, 9.49; N, 2.59. Found: C, 72.88; H, 9.27; N, 2.70.

3β,26-Dihydroxy-16β,22-imino-5,16,20(22)-cholestatriene (III). A solution of 10 g. of kryptogenin in 100 ml. of ethyl alcohol and 50 ml. of liquid ammonia was heated at 135° and 480 p.s.i. for 4 hr. in an autocalve. The cooled solution was treated with Norite, filtered and concentrated at room temperature under nitrogen and *in vacuo*. The residual yellow glass crystallized from 50 ml. of ice cold acetone to yield 6.64 g. of the product as rosettes of white needles, m.p. 197–199° (*in vacuo*). The analytical sample melted at 201–204° (*in vacuo*), $[\alpha]_D$ −249°, $\lambda_{max}^{CH_3OH}$ 206 mμ, ε 3950; 236 mμ, ε 243; $\lambda_{max}^{CH_3OH+HCl}$ 206 mμ, ε 5060.

Anal. Calcd. for $C_{27}H_{41}NO_2$: C, 78.78; H, 10.04; N, 3.40. Found: C, 78.48; H, 9.78; N, 3.31.

Attempts to prepare this product by heating kryptogenin at 135° in molten ammonium acetate always gave a reaction of some sort, obvious from the appearance of the mixture, but yielded products which were either insoluble in ether or of low nitrogen content.

3β,26-Dihydroxy-16β,22-methylimino-5,16,20(22)-cholestatriene (IV). Acetic acid, 103.2 g., and 153 g. of 35% aqueous methylamine were cautiously mixed, 5.0 g. of kryptogenin added, and the whole heated, with distillation and stirring at 120–130° for 90 min. At one time the mixture became quite viscous although this effect shortly subsided. After standing overnight the mixture was still fluid but contained solid material. Dilution, filtration, washing, and drying *in vacuo* gave 4.75 g. of a greenish-white powder, m.p. 190–195° (with browning); 220–222° (*in vacuo* with shrinking at 205°). Crystallization of small amount was performed three times using ethyl alcohol and a nitrogen atmosphere as much as possible. The product crystallized as micro needles, m.p. 223–224° (*in vacuo*), $[\alpha]_D$ −67° (chloroform solution darkened on standing), $\lambda_{max}^{CH_3OH}$ 206 mμ, ε 11,850; 236 mμ, ε 9,450; $\lambda_{max}^{CH_3OH+HCl}$ 206 mμ, ε 8850; 278 mμ, ε 14,800.

Anal. Calcd. for $C_{28}H_{43}NO_2$: C, 79.01; H, 10.18; N, 3.29. Found: C, 78.53; H, 10.08; N, 3.26.

3β,26-Dihydroxy-16β,22-methylimino-5-cholestene (V). A. A mixture of 80 g. of formic acid and 153 g. of 35% aqueous methylamine was prepared with chilling in a three-necked flask bearing a stirrer, immersion thermometer and distillation tubulature. After addition of 3.0 g. of 3β,26-dihydroxy-16,22-methylimino-5,16β,20(22)-cholestatriene heat was applied. At 115° gas evolution became apparent accompanied by serious foaming which was difficult to control. A lime-water test showed the gas to be carbon dioxide. After 2 hr. the temperature reached 132° where foaming was again a problem. After 5 hr. the temperature reached 140° where it was held for another 0.5 hr. (At one time the tubulature was washed down with a little water. This reduced the internal temperature for a time and caused the mixture to assume a dark prussian blue color.) The resulting dark solution deposited crystals on standing overnight. These were collected and dried giving 1.87 g. of bronze plates, m.p. 195–210°. This was starting material, as shown by melting point, rotation, and infrared and ultraviolet spectra of a purified sample.

The dark blue aqueous filtrate was mixed with 250 cc. of 50% potassium hydroxide, the whole extracted with ether, and the ethereal solution washed, dried, and evaporated. Recrystallization of the dark residue twice from methyl alcohol and once from ethyl acetate yielded 0.6 g. of the pyrrolidine, m.p. 215.0–215.5° (*in vacuo*), identical with the product described below.

B. A mixture of 153 g. of 35% aqueous methylamine and 80 g. of formic acid was prepared in a 1-l. flask arranged for stirring and distillation. Addition of 5.0 g. of kryptogenin and heating to 125° caused the sudden appearance of a foam coated with a steel-gray solid. Foam formation with evolution of carbon dioxide was so vigorous that stirring and heating were discontinued periodically as necessary. After

(10) R. E. Marker, *et al.*, *J. Am. Chem. Soc.*, 69, 2167 (1947).

(11) We thank Dr. Monroe E. Wall of the Eastern Regional Laboratories, U. S. Department of Agriculture, Philadelphia 18, Pa., for examining our material and confirming our identification of it.

eight or ten such manipulations during 2–3 hr., the internal temperature could be raised to 132° where it was held without further incident for 30 min. The gray solid was collected, washed with water, and dried; it weighed 3.55 g., m.p. 203–207° (air). Recrystallization from ethyl alcohol was accompanied by darkening of the solutions and consequent losses of material. However, by the judicious use of charcoal and filter aid the pure pyrrole IV was obtained, m.p. 223.2–224.3°, $[\alpha]_D$ −58°, identical in spectra and analyses with that obtained from kryptogenin and methylammonium acetate.

The aqueous filtrate from the reaction was treated with 250 ml. of 33% potassium hydroxide and extracted with ether. The washed and dried ethereal solution was evaporated, leaving 1.41 g. of crystalline material. This was the *N*-methylpyrrolidine V, crystallizing from ethyl acetate as needles, m.p. 214.0–215.2° (*in vacuo*), $[\alpha]_D$ −54°.

Anal. Calcd. for $C_{28}H_{47}NO_2$: C, 78.27; H, 11.03; N, 3.26. Found: C, 78.20; H, 10.85; N, 3.33.

Acetylation was accomplished by boiling 0.1 g. of the pyrrolidine in 5 ml. of acetic anhydride for 30 min. and isolating the product with water and ether at room temperature. The resultant oil crystallized on standing for a few minutes. It was recrystallized from aqueous methyl alcohol five times to remove all color. The diacetate of V crystallized as plates, m.p. 98.5–100.4°.

Anal. Calcd. for $C_{32}H_{51}NO_4$: C, 74.81; H, 10.01; N, 2.73. Found: C, 74.92; H, 9.83; N, 2.68.

The methiodide was prepared by warming 0.48 g. of V, 100 ml. of chloroform and 30 ml. of methyl iodide in a pressure bottle at 70° for 4 hr. The solution was concentrated under nitrogen to 30 ml., cooled and a solid collected which was triturated with 10 ml. of boiling chloroform, giving 0.50 g. of the crystalline methiodide, m.p. 269–271°. The analytical sample was recrystallized twice from isopropyl alcohol and melted at 273.5–275.0°, $[\alpha]_D$ −25° (1% in methanol).

Anal. Calcd. for $C_{29}H_{50}INO_2$: C, 60.93; H, 8.82; N, 2.45; I, 22.20. Found: C, 60.78; H, 8.59; N, 2.33; I, 21.70.

3β,26-Dihydroxy-16β,22-ethylimino-5-cholestene. Kryptogenin, 4.3 g., was treated with a mixture of 65.5 ml. of formic acid and 77.5 g. of ethylamine, the whole being heated with stirring at 105° until distillation ceased, cooled and treated with 200 ml. of 5% sodium hydroxide. Chloroform extracts of this solution were washed, dried and evaporated, yielding a semisolid crystallizing well from methanol to yield 1.25 g. of the product. An analytical sample recrystallized from ethyl acetate melted at 163–167°, $[\alpha]_D$ −71°.

Anal. Calcd. for $C_{29}H_{29}NO_2$: C, 78.50; H, 11.13; N, 3.16. Found: C, 78.17; H, 10.75; N, 3.18.

3β,26-Dihydroxy-16β,22-iminocholestane (VI). *A. From 3β,26-dihydroxy-16β,22-imino-5-cholestene,* II. A solution of 100 mg. of platinum oxide is approximately 6 ml. of glacial acetic acid was prehydrogenated in a hydrogen atmosphere at 25°. Then 100 mg. of II in glacial acetic acid was added to the hydrogenation vessel. After 4–5 hr. 6.7 ml. of hydrogen was absorbed (theory for 1 mole, 5.4 ml.). The mixture was filtered and evaporated *in vacuo* at 40–50°, the resulting residue being treated with 100 ml. of 1.5*N* ammonium hydroxide and then extracted three times with a mixture of chloroform and ethyl ether (1:3). The combined organic extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated *in vacuo* to give 114 mg. of crude product, m.p. 172–176°. Crystallization from ethyl acetate gave 71 mg. of VI, m.p. 174.5–177°, $[\alpha]_D$ +12.5°

B. *From 3β,26-dihydroxy-16β,22-imino-5,16,20(22)-cholestatriene,* III. A solution of 100 mg. of III in glacial acetic acid, hydrogenated as described above, absorbed 16.8 ml. of hydrogen (theory for 3 moles, 16.4 ml.). Processing the mixture as just described yielded 116 mg. of crude material, m.p. 168–173°. Crystallization from ethyl acetate gave 76 mg. of VI, m.p. 174–176°, $[\alpha]_D$ +12.5°.

A mixture of the two preparations melted at 174–177°. Uhle and Sallmann[2] give the constants, m.p. 174–177°, $[\alpha]_D$ +18°.

SKOKIE, ILL.

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CIBA PHARMACEUTICAL PRODUCTS, INC.]

Mannich Bases Prepared from Steroids

GEORGE DESTEVENS AND ANGELA HALAMANDARIS

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The Mannich reaction has been applied to various steroidal compounds. The 3-ketoandrostane derivatives react under the usual conditions to yield methylene-2,2′-bis(ketoandrostanes). A method has been worked out for preparing the 2-substituted Mannich bases of 3-ketoandrostanes and 3-keto-Δ^4-androstenes.

Although the Mannich reaction has been employed extensively for the preparation of α-substituted cyclic ketones,[1] its application to steroidal ketones is limited to a report by Julian,[2] *et al.*, on the preparation of 16-dimethylaminomethyldehydroisoandrosterone. Our recent interest in the preparation of Mannich bases as intermediates[3] in the synthesis of pharmacologically active compounds prompted us to study this reaction in more detail in the steroid series. Moreover, it may also offer another method for the synthesis of the biologically important 2-methyl derivatives.[4]

Initially, 17β-propionoxy-5α-androstan-3-one (I) was allowed to react with dimethylamine hydrochloride and 37% aqueous formaldehyde in boiling ethyl alcohol, relatively mild conditions for a Mannich reaction. After refluxing the solution for three hours, a precipitate began to form which became more copious with continued reflux. The white flocculent substance, m.p. 250–252°, was found to be devoid of nitrogen and had an analysis agreeing well for a compound of empirical formula $C_{45}H_{68}O_6$. The ultraviolet absorption spectrum gave

(1) F. F. Blicke, *Org. Reactions* I, 303 (1942).

(2) P. L. Julian, E. W. Meyer, and A. C. Printy, *J. Am. Chem. Soc.*, **70**, 3872 (1948).

(3) G. deStevens, A. F. Hopkinson, M. A. Connelly, P. Oke, and D. C. Schroeder, *J. Am. Chem. Soc.*, **80**, 2201 (1958).

(4) H. J. Ringold, E. Batres, O. Halpern, and E. Necoechea, *J. Am. Chem. Soc.*, **81**, 427 (1959).