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°, [α]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*), [α]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°, [α]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°, [α]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°, [α]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°, [α]D +12.5°.

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

SKOKIE, ILL.

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

Mannich Bases Prepared from Steroids

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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

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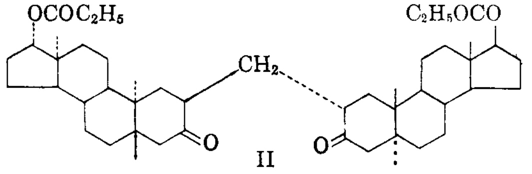
(1) F. F. Blicke, *Org. Reactions* I, 303 (1942).

(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).

one maximum of low intensity ($E^{1\%}_{1cm}$ = 23.70) at 248 mμ, thus eliminating the possibility of an α,β-unsaturated ketone. Infrared spectroscopy revealed a band at 1740 cm.$^{-1}$ for the ester grouping and strong carbonyl absorption at 1725 cm.$^{-1}$ The molecular weight of the substance according to the Rast method was found to be 670. Structure II, methylene-2,2′-bis(17-β-propionoxy-5α-androstan-3-one), satisfies all these data. This compound can be conceivably formed by breakdown of the initially formed Mannich derivative to the corresponding 2-methylene compound which undergoes Michael addition to another molecule of 17β-propionoxy-5α-androstan-3-one.[5] However, it is also possible that the 2-methylene derivative can condense at C_4 of I, even though enolization toward C_2 is favored in the steroid ketones of the *trans* A/B type. Recently, Barton,[6] has reported that 2α-methylcholestanone does not condense at all with benzaldehyde, indicating no tendency for C_4 condensation when C_2 is blocked. We carried out this benzaldehyde condensation reaction with methylene-2,2′-bis(17β-hydroxy-5α-androstan-3-one) III. Work up of the reaction gave back exclusively starting material indicating that our methylene linkages are at C_2.



II

Finally compound III and methylene-2,2′-bis(cholestan-3-one) IV condensed with two molecular equivalents of 2,4-dinitrophenylhydrazine which indicates that each of these compounds contains two carbonyl groups.

On the other hand, coprostan-3-one when refluxed for twenty-four hours in ethyl alcohol with dimethylamine hydrochloride and formaldehyde yielded only a small amount of the presumably 4β-dimethylaminomethyl coprostan-3-one (V). The steric influence of the axial hydrogen at C_7 may be significant in this case. Also, it was observed that 3-acetoxy-6-ketocholestane was inert to these reaction conditions. Similar to Julian's[2] findings, a 10% yield of 3β-methoxy-16-dimethylaminomethyl-5α-androstan-17-one hydrochloride (VI) was obtained on refluxing an ethyl alcohol solution of the 17-ketone with dimethylamine hydrochloride and formaldehyde.

Various transformations leading to the 2-substituted Mannich bases of 17β-hydroxy-5α-androstan-3-one are outlined in Scheme I. It was found that dimerization could be prevented if the reactions were carried out at room temperature. For instance, allowing VIII to stand at room temperature with dimethylamine hydrochloride and formaldehyde for a twenty-four hour period gave a 5% yield of IX whereas after one week the yield was increased to 30%. However, treatment of IX with an equivalent amount of 17β-hydroxy-5α-androstan-3-one in ethyl alcohol under reflux gave rise again to III. Reaction of I with pyrrolidine hydrochloride and formaldehyde at room temperature gave a 35% yield of 2α-pyrrolidinomethyl 17β-hydroxy-5α-androstan-3-one (XI). Compound XI was also prepared by a route which definitely establishes that Mannich condensation with 5α-androstan-3-ones occurs at C_2 rather than C_4. 2-Hydroxymethylene-17β-hydroxy-5α-androstan-3-one (VII)[7] was allowed to condense with pyrrolidine to give the enamine X which underwent reduction with lithium aluminum hydride *via* 1,4-addition to a compound which was identical in all respects with XI. Finally, 2α-pyrrolidinomethyltestosterone (XIV) prepared by a similar sequence of reactions from testosterone,[8] was reduced with lithium-liquid ammonia. Once again compound XI was formed. The α-orientation assigned follows from the nature of the hydride reduction. In such 1,4-additions a *quasi*-planar enolate intermediate is formed followed by hydrogen addition from the less hindered side.[9] This is further supported by the fact that XI was not isomerized by treatment with sodium methoxide in methanol.[10] The methiodide salts of XI prepared by the three different routes were identical.

EXPERIMENTAL

Methylene-2,2′-bis(17β-propionoxy-5α-androstan-3-one (II). A solution of 7.0 g. of 17β-propionoxy-5α-androstan-3-one, 1.6 g. of dimethylamine hydrochloride, and 2 ml. of 37% aqueous formaldehyde was refluxed for 16 hr. The copious precipitate was filtered and washed well with ethyl alcohol. The substance was found to be highly insoluble in most organic solvents. One recrystallization from ethyl alcohol gave 2.5 g. of an analytically pure sample, m.p. 250–252°, $(\alpha)^{27°}_{D}$ +53.34 (chloroform), $\lambda^{C_2H_5OH}_{max}$ 248 mμ ($E^{1\%}_{1\,cm}$ = 23.70), infrared spectrum:[11] 1740 cm.$^{-1}$ (—C=O), 1725 cm.$^{-1}$

Anal. Calcd. for $C_{45}H_{68}O_6$: C, 76.75; H, 9.66; mol, wt., 704.6. Found: C, 76.72; H, 9.64; mol. wt., 670 (Rast).

Methylene-2,2′-bis(17β-hydroxy-5α-androstan-3-one) (III). 17β-Hydroxy-5α-androstan-3-one (5.8 g.) was allowed to react under reflux in 50 ml. of ethyl alcohol with 1.6 g. of dimethylamine hydrochloride and 2 ml. of 37% aqueous

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[5] Such condensations involving Mannich derivatives were first developed by R. Robinson, *J. Chem. Soc.*, 53 (1937). More recently, this type of dimerization was found to occur when the Mannich reaction was carried out with 2-phenylindole. *Cf.* R. Dahlbom and A. Miscorny, *J. Am. Chem. Soc.*, **82**, 2397 (1960).

[6] D. H. R. Barton, F. McCapra, P. J. May, and F. Thudium, *J. Chem. Soc.*, 1297 (1960).

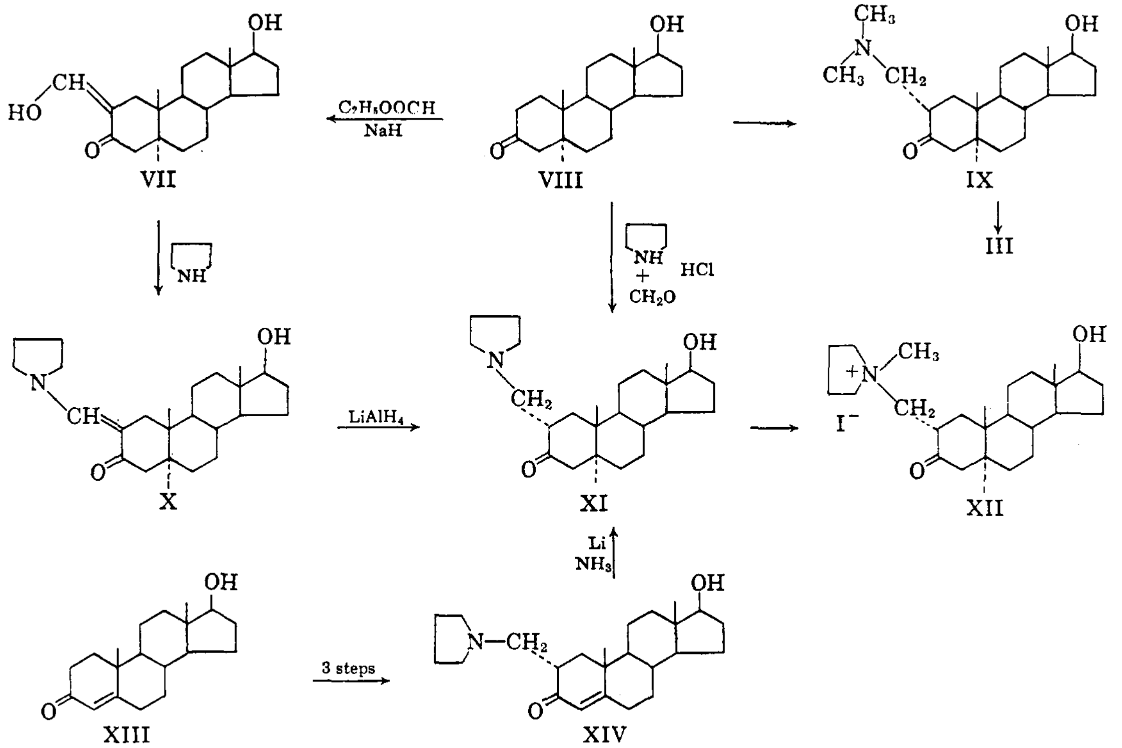
[7] F. L. Weisenborn and H. E. Applegate, *J. Am. Chem. Soc.*, **81**, 1960 (1959).

[8] J. Meier, *Chimia*, **13**, 65 (1959).

[9] (a) N. G. Gaylord, *Reduction with Complex Metal Hydrides*, Interscience, New York, 1956, pp. 149–166; 180–182. (b) D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 44 (1956).

[10] J. A. Hogg, F H. Lincoln, R. W. Jackson, and W. P. Schneider, *J. Am. Chem. Soc.*, **77**, 6401 (1955).

[11] All spectra were run in Nujol.



formaldehyde for a period of 16 hr. The precipitate was filtered, washed with ethyl alcohol and then recrystallized from alcohol. The pure material melted at 260–262°, $(\alpha)_D^{27°}$ = +70.26 (chloroform), $\lambda_{max}^{C_2H_5OH}$ 245 mμ (ε = 1000), infrared spectrum: 3536 cm.$^{-1}$, 3472 cm.$^{-1}$ (—OH); 1715 cm.$^{-1}$ (—C=O).

Anal. Calcd. for $C_{39}H_{60}O_4$: C, 78.87; H, 10.20. Found: C, 78.98; H, 10.03.

The 2,4-dinitrophenylhydrazone of III crystallized from ethyl alcohol as tiny orange cubes, m.p. 330–334°.

Anal. Calcd. for $C_{51}H_{68}N_8O_{10}$: N, 11.78. Found: N, 11.70.

Compound III (50 mg.) was treated with benzaldehyde in 0.1*N* ethanolic potassium hydroxide (50 ml.). Forty-five milligrams of starting material was isolated after 48 hr.

Methylene-2,2'-bis(cholestan-3-one) (IV). Fifty milliliters of ethyl alcohol containing 7.9 g. cholestan-3-one, 1.8 g. dimethylamine hydrochloride, and 3 ml. of 37% aqueous formaldehyde was refluxed for 16 hr. after which time the copious precipitate was collected and recrystallized from ethyl alcohol. The yield of white flocculant substance, m.p. 218–220° was 5 g. $(\alpha)_D^{27°}$ +65.52 (chloroform), infrared spectrum: strong 1730 cm.$^{-1}$ and medium weak 1710 cm.$^{-1}$

Anal. Calcd. for $C_{55}H_{92}O_2$: C, 84.30; H, 11.53. Found: C, 84.23; H, 11.53.

The 2,4-dinitrophenylhydrazone derivative of IV melted at 302°.

Anal. Calcd. for $C_{67}H_{100}N_8O_8$: N, 9.75. Found: N, 9.50.

4β-Dimethylaminomethyl coprostan-3-one hydrochloride (V). Coprostan-3-one (200 mg.) was dissolved in 10 ml. of ethyl alcohol containing 47 mg. of dimethylamine hydrochloride and 0.2 ml. of 37% aqueous formaldehyde. The solution was refluxed on a steam bath for 20 hr. The alcohol was removed under reduced pressure and the residue was taken up in 50 ml. of water. Some unchanged coprostan-3-one did not dissolve in water. After filtration, the filtrate was made alkaline then extracted with ether and dried over sodium sulfate. The extract was filtered and treated with 4 drops of ethyl alcohol saturated with hydrogen chloride. The white precipitate was collected and dried *in vacuo* overnight; yield: 5 mg.; 163–164°.

Anal. Calcd. for $C_{30}H_{44}ClNO$: C, 76.82; H, 9.39. Found: C, 76.65; H, 9.52.

3β-Methoxy-16-dimethylaminomethyl-5α-androstan-17-one hydrochloride (VI). 3β-Methoxy-5α-androstan-17-one, (3.04 g.), 0.81 g. of dimethylamine hydrochloride, and 2 ml. of 37% aqueous formaldehyde were dissolved in 25 ml. of ethyl alcohol. The solution was refluxed for 24 hr. The ethyl alcohol was removed *in vacuo* and the residue was triturated with 100 ml. of water. After filtration, the filtrate was made basic with sodium bicarbonate solution. The resulting turbid solution was extracted with ether and the ether extract dried over sodium sulfate. After filtering off the salt, the ether filtrate was treated with ethyl alcohol saturated with hydrogen chloride. A 10% yield of product was obtained which was recrystallized from alcohol-ether. The analytically pure sample melted at 190–191°. $\lambda_{max}^{C_2H_5OH}$ 294 mμ (ε 776), infrared spectrum: 2643 cm.$^{-1}$, 2485 cm.$^{-1}$ (—N$^+$—H); 1743 cm.$^{-1}$ (s) (—C=O); 1100 cm.$^{-1}$ (s) (C—O—C).

Anal. Calcd. for $C_{23}H_{40}ClNO_2$: C, 69.73; H, 10.10; N, 3.53. Found: C, 70.05; H, 10.21; N, 3.52.

2α-Dimethylaminomethyl-17β-hydroxy-5α-androstan-3-one hydrochloride (IX). Five and one-half grams of 17β-hydroxy-5α-androstan-3-one (VIII), dissolved in 50 ml. of ethyl alcohol, was treated with 1.6 g. of dimethylamine hydrochloride and 2 ml. of 37% aqueous formaldehyde. After 4 hr. at room temperature, the reaction mixture was treated as described in the previous example to give 0.32 g. (5%) of product. When the reaction mixture was allowed to stand at room temperature for 1 week a 30% yield (1.9 g.) of product was obtained, m.p. 168°, $(\alpha)_D^{25°}$ = +5.42 (chloroform), infrared spectrum: 3363 cm.$^{-1}$ (s) (—OH); 1710 cm.$^{-1}$ (—C=O); 2350–2700 cm.$^{-1}$ (—N$^+$—H). The analysis indicated that this compound contained 1 mole of water of crystallization.

Anal. Calcd. for $C_{22}H_{37}ClNO_2.H_2O$: C, 66.05; H, 9.95; N, 3.50. Found: C, 66.37; H, 10.30; N, 3.51.

The above substance was allowed to react with an equivalent amount of 17β-hydroxy-5α-androstan-3-one in ethyl alcohol under reflux to form the dimer III.

2α-Pyrrolidinomethyl-17β-hydroxy-5α-androstan-3-one hydrochloride (XI). The ketone VIII (2.75 g.), dissolved in 25 ml. of ethyl alcohol, was treated with 1.07 g. of pyrrolidine hydrochloride and 2 ml. of 37% aqueous formaldehyde and was allowed to stand at room temperature for 1 week. Work up in the usual manner gave 1.4 g. of pure amine hydrochloride XI, m.p. 198–200°, $(\alpha)^{27°}_{D} = -0.17$, infrared spectrum: broad 3297 cm.$^{-1}$ (—OH); 2700–2400 cm.$^{-1}$ (—N^{+}—H); 1719 cm.$^{-1}$ (s) (—C═O).

Anal. Calcd. for $C_{24}H_{40}ClNO_2$: C, 70.30; H, 9.76. Found: C, 69.90; H, 9.89.

The free base (0.5 g.) of the above compound was dissolved in 10 ml. of acetone and then treated with 1 g. of methyl iodide. An immediate reaction occurred followed by the precipitation of the *2α-pyrrolidinomethyl-17β-hydroxy-5α-androstan-3-one methiodide* (XII). Recrystallization from ethyl alcohol yielded white crystalline substance, m.p. 248–250°, $(\alpha)^{27°}_{D}$ 3.72 (methyl alcohol), infrared spectrum: 3404 cm.$^{-1}$ (—OH); 1714 cm.$^{-1}$ (—C═O).

Anal. Calcd. for $C_{25}H_{42}INO_2$: C, 58.24; H, 8.21. Found: C, 58.24; H, 8.20.

2-(Pyrrolidinomethylene)-17β-hydroxy-5α-androstan-3-one (X). Ten grams of 2-hydroxymethylene-17β-hydroxy-5α-androstan-3-one[7] (VII) was dissolved in 500 ml. of dry benzene. Five grams of pyrrolidine were added and the solution was refluxed for 4 hr. as the water formed was collected in a water trap. The benzene was then removed *in vacuo* and the residue was recrystallized from ethyl acetate–ethyl alcohol. The resulting yellow crystals melted at 280–281°, $(\alpha)^{27°}_{D} = -124.86$ (chloroform), $\lambda_{max}^{C_2H_5OH}$ 339 mμ (ε 23,750), infrared spectrum: 3390 cm.$^{-1}$ (—OH); 1624 cm.$^{-1}$ (N—C═C).

Anal. Calcd. for $C_{24}H_{37}NO_2$: C, 77.58; H, 10.02; N, 3.78. Found: C, 77.66; H, 10.24; N, 3.82.

Reduction of X *to* XI. Compound X (4.5 g.) dissolved in 100 ml. of tetrahydrofuran was added slowly to a suspension of 3.5 g. of lithium aluminum hydride in 200 ml. of ether in a 1 l. flask connected with a stirrer, dropping funnel, and reflux condenser; the mixture was refluxed for 3 hr. A saturated solution of sodium potassium tartrate was added slowly to the solution. The mixture was filtered and the filtrate was extracted with ether and methylene chloride. The combined extract dried over magnesium sulfate, was filtered, and the filtrate evaporated to dryness *in vacuo*. The residue was taken up in a small amount of ethyl alcohol and then treated with ethyl acetate saturated with hydrogen chloride gas. The resulting viscous material was triturated well with ether and then recrystallized twice from ethyl alcohol–ether acetone to give one gram of product, m.p. 200°. This substance was identical with compound XI prepared *via* the Mannich reaction. The two samples gave superimposable infrared spectra and mixture melting point gave no depression.

The methiodide salt (m.p. 250–251°) of this compound was also identical with XII.

Anal. Calcd. for $C_{25}H_{42}INO_2$: C, 58.24; H, 8.21. Found: C, 58.20; H, 8.14.

Reduction of 2α-pyrrolidinomethyltestosterone XIV *to* XI. 2α-Pyrrolidinomethyltestosterone[8] (0.5 g.) prepared *via* the enamine intermediate was dissolved in a mixture of 12 ml. of dry dioxane and 6 ml. of dry ether. This solution was then added over a 10-min. period to a solution of 100 mg. of lithium dissolved in 50 ml. of liquid ammonia. An additional 50 mg. of lithium was added to maintain the blue color for an additional 30 min. The lithium amide formed was neutralized by the addition of 1.2 g. of ammonium chloride and the ammonia was allowed to evaporate. The residue was dissolved in chloroform, the solution was washed with water, dried over sodium sulfate and concentrated *in vacuo*. The resulting solid was dissolved in a small amount of ethyl alcohol and treated with ethyl acetate saturated with hydrogen chloride; a semicrystalline substance was obtained which was recrystallized from ethyl alcohol–ether to yield 90 mg. of substance, m.p. 198–200°, identical in all respects with XI.

The free base of XI (0.5 g.) was treated with sodium methoxide (0.3 g.) dissolved in 50 ml. of methanol for 2 hr. The starting material was recovered quantitatively.

Acknowledgment. We would like to take this opportunity to thank Dr. Schlittler for his interest and encouragement. We are indebted to Mr. Louis Dorfman and his microanalytical group for their diligent cooperation.

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[CONTRIBUTION FROM THE LABORATORY OF CHEMISTRY OF NATURAL PRODUCTS, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH, U. S. PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

Haemultine and the Alkaloids of *Haemanthus multiflorus* Martyn[1]

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An investigation of the alkaloids of *Haemanthus multiflorus* Martyn has shown the presence of lycorine and montanine. No haemultine, previously reported by other workers to occur in this source, could be detected. Demethoxylation of either crinamine or haemanthamine with sodium and amyl alcohol affords two isomeric demethoxy derivatives (II and III) as well as the respective dihydro compounds.

A previous investigation of the alkaloids of *Haemanthus multiflorus* Martyn reported the presence of chlidanthine, haemanthidine, haemultine, hippeastrine and lycorine.[2a,2b] Of these alkaloids, only haemultine was of unknown structure. This alkaloid, $C_{16}H_{17}NO_3$, contained a basic, tertiary nitrogen, one reducible double bond, one hydroxyl and one methylenedioxy group. The hydroxyl was considered to be located in a five-membered ring and secondary since dihydrohaemultine was oxidized by chromic acid to a ketone hydroiodide showing absorption at 5.71 μ (1751 cm.$^{-1}$). It was reported that haemultine was obtained also from the action of sodium and *n*-amyl alcohol on either haemanthamine or crinamine.[2a] With the determination of the structures of

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(1) Paper XXI on the alkaloids of the Amaryllidaceae; previous paper, H. M. Fales and W. C. Wildman, *J. Org. Chem.*, **26**, 881 (1961). For a recent review of the alkaloids of this family, see W. C. Wildman in *The Alkaloids*, R. H. Manske, ed., Academic Press, New York, 1960, Vol. VI, p. 289.

(2)(a) H.-G. Boit and W. Döpke, *Chem. Ber.*, **91**, 1965 (1958); (b) H.-G. Boit, W. Döpke, and W. Stender, *Naturwissenschaften*, **45**, 390 (1958).