7-Keto-17α-ethylandrostenediol (XVIIIb).—To a solution of 4 g. of the 3-monoacetate XVIIIa in 135 ml. of 1:2 dioxane–methanol was added 18.5 ml. of aqueous 2 *N* potassium hydroxide. The mixture was stored for 3 hr. at 25°, acidified with dilute acetic acid and poured into an excess of cold 3% brine. The precipitate was collected, washed and air-dried to give 3.6 g. of crude product. Crystallization from 10:1 ethyl acetate–acetone provided 3.15 g., m.p. 226–228°. Recrystallization from acetone afforded pure XVIIIb, m.p. 227–229°, $[\alpha]_D$ −161° (1.04% in $CHCl_3$), $\epsilon_{2375}^{CH_3OH}$ 12,500; μ^{KBr} 2.90 (shoulder), 2.95, 6.04 and 6.15.

Anal. Calcd. for $C_{21}H_{32}O_3$ (332.47): C, 75.86; H, 9.70. Found: C, 75.92; H, 9.91.

Pregna-3,5-diene-7,20-dione (XIX).[27]—A solution of 20 g. of 3β-acetoxypregn-5-ene-7,20-dione (III)[3a,d,5] in 400 ml. of 95% ethanol was treated with 10 ml. of 12 *N* hydrochloric acid and heated under nitrogen and reflux for 2 hr. After precipitation with cold water, filtration and air-drying, there was found 17.5 g. of light yellow powder. Crystallization from methanol gave 9.96 g., m.p. 155–160°. Two recrystallizations provided pure XIX, m.p. 159–161°, $[\alpha]_D$ −297° (1.15% in $CHCl_3$), $\epsilon_{2790}^{CH_3OH}$ 21,200; μ^{KBr} 5.90, 6.08, 6.20 and 6.32.

Anal. Calcd. for $C_{21}H_{28}O_2$ (313.41); C, 80.73; H, 9.03. Found: C, 80.71; H, 9.03.

17α-Acetoxypregna-3,5-diene-7,20-dione (XX).—To a solution of 4.15 g. of 3β,17α-diacetoxypregn-5-ene-7,20-dione (IV) in 60 ml. of acetic acid was added 0.30 g. of *p*-toluenesulfonic acid monohydrate. The mixture was refluxed for 50 minutes, chilled and 72 ml. of cold water slowly added with stirring. The crystalline precipitate was filtered, washed and dried to give 3.03 g., m.p. 230–231°. Two recrystallizations from ethyl acetate furnished pure XX, m.p. 234–236°, $\epsilon_{2780}^{CH_3OH}$ 21,700; μ^{KBr} 5.77, 5.82 (shoulder), 6.05, 6.17, 6.28, 7.94 and 8.16.

Anal. Calcd. for $C_{23}H_{30}O_4$ (370.47): C, 74.56; H, 8.18. Found: C, 74.56; H, 8.25.

17α-Hydroxypregna-3,5-diene-7,20-dione (XXIII).—To a solution of 1.5 g. of the 7-keto-diene 17α-acetate XX in 150 ml. of 1:2 dioxane–methanol, was added 20 ml. of aqueous 2 *N* potassium hydroxide. Aliquots of the reaction mixture were titrated at intervals, and, after 4.5 hr., 0.94 equivalent of base had been consumed. After another 15 minutes, the mixture was acidified with cold dilute acetic acid and poured into cold 5% brine. The precipitate was filtered, washed and air-dried to give 1.02 g., m.p. 217–218°. Two recrystallizations from ethyl acetate afforded pure XXIII, m.p. 223–224°, $[\alpha]_D$ −387° (0.89% in $CHCl_3$), $\epsilon_{2775}^{CH_3OH}$ 22,600; μ^{KBr} 2.95, 5.86, 6.10, 6.20 and 6.30.

Anal. Calcd. for $C_{21}H_{28}O_3$ (328.43): C, 76.79; H, 8.59. Found: C, 76.87; H, 8.69.

21-Acetoxypregna-3,5-diene-7,20-dione (XXI).—To a solution of 1 g. of 3β,21-diacetoxypregn-5-ene-7,20-dione (IXa) in 20 ml. of acetic acid was added 120 mg. of *p*-toluenesulfonic acid monohydrate. The mixture was heated under reflux for 1 hr., chilled and 30 ml. of cold water slowly added with stirring. The crystalline precipitate was filtered, washed with cold water and dried to 0.79 g., m.p. 170–172°. Two recrystallizations from acetone–methanol provided pure XXI, m.p. 173–174°, $[\alpha]_D$ −219° (1.02% in $CHCl_3$), $\epsilon_{2780}^{CH_3OH}$ 22,400; μ^{KBr} 5.70, 5.80, 6.05, 6.16, 6.27 and 8.12.

Anal. Calcd. for $C_{23}H_{30}O_4$ (370.47): C, 74.56; H, 8.16. Found: C, 74.32; H, 8.05.

17α,21-Diacetoxypregna-3,5-diene-7,20-dione (XXII).—To a solution of 8 g. of 3β,17α,21-triacetoxypregn-5-ene-7,20-dione (Xa) in 120 ml. of acetic acid, was added 0.6 g. of *p*-toluenesulfonic acid monohydrate. The mixture was heated under reflux for 1 hr., chilled and 140 ml. of cold water slowly added with stirring. The crystalline precipitate was filtered, washed with cold water and dried to 6.14 g. Recrystallization from methanol gave 5.22 g., m.p. 234–235°. Two recrystallizations provided pure XXII, m.p. 241–242°, $[\alpha]_D$ −313° (1% in $CHCl_3$), $\epsilon_{2785}^{CH_3OH}$ 23,600; μ^{KBr} 5.70, 5.76–5.78 (broad), 6.07, 6.18, 6.30, 8.0 (shoulder), 8.09 and 8.17.

Anal. Calcd. for $C_{25}H_{32}O_6$ (428.51): C, 70.07; H, 7.53. Found: C, 69.82; H, 7.40.

17α,21-Dihydroxypregna-3,5-diene-7,20-dione (XXIV).—To a solution of 5 g. of the 7-keto-diene diacetate XXII in 140 ml. of 9:5 dioxane–methanol under nitrogen at 25°, and with stirring, was added 150 ml. of methanolic 0.16 *N* potassium hydroxide. After 4 minutes, 1 ml. of water was added. After another 5 minutes, the mixture was chilled, acidified with dilute acetic acid and poured into cold 5% brine. The precipitate was filtered, washed and air-dried to give 3.80 g. of powder. Crystallization from ethyl acetate and from acetone gave 2.80 g. of crude product in four crops, m. range 202–212°. Two recrystallizations from methanol furnished pure XXIV, m.p. 216-216.5°, $[\alpha]_D$ −338° (1.15% in $CHCl_3$), $\epsilon_{2780}^{CH_3OH}$ 23,200; μ^{KBr} 2.90, 2.96, 5.84, 6.11, 6.20 and 6.30.

Anal. Calcd. for $C_{21}H_{28}O_4$ (344.43): C, 73.23; H, 8.19. Found: C, 73.20; H, 8.14.

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(27) References 3a and 5. These authors mention this structure but give no experimental data nor characteristics.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Steroidal Hormone Analogs. I. Synthesis of 18,19-Dinorprogesterone and 14-Hydroxy-18,19-dinorprogesterone[1]

BY NORMAN A. NELSON AND ROBERT B. GARLAND[2]

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The total synthesis of 14-hydroxy-18,19-dinorprogesterone (14-hydroxy-18,19-dinorpregn-4-ene-3,20-dione) is described. A by-product at one point in the synthesis of this substance was used in the preparation of 18,19-dinorprogesterone (18,19-dinorpregn-4-ene-3,20-dione). Conversion of 1-keto-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene to the hormone analogs utilized the method of attachment of ring D recently described by Sarett and co-workers in their synthesis of cortisone. The stereochemistry of the two products is discussed and it is felt that in each case the configuration corresponds to that of natural progesterone.

In recent years a number of 3-keto-Δ^4-19-nor-steroidal hormones have been prepared.[3-5] In most instances the 19-nor analogs have similar but

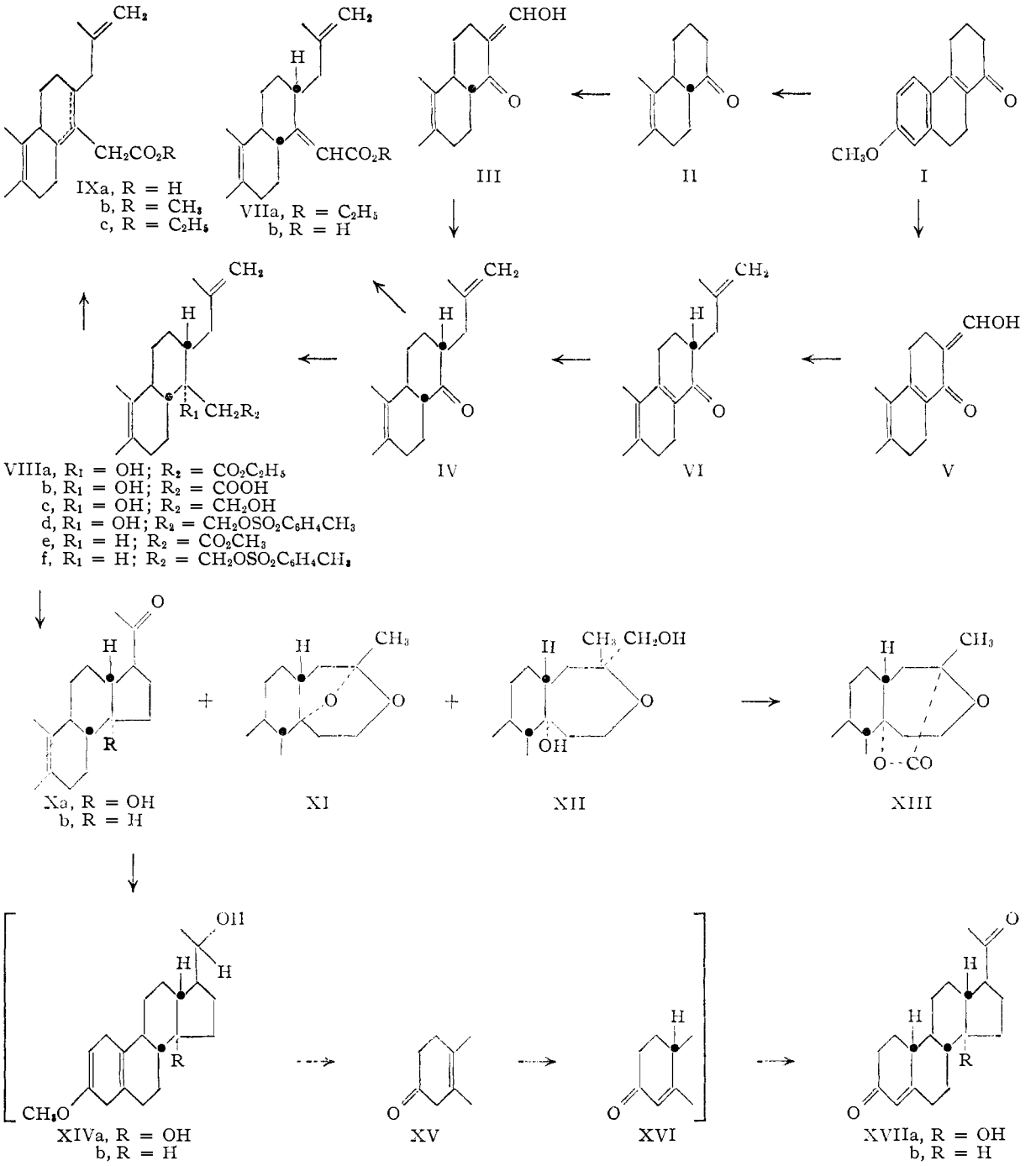
(1) Abstracted from the thesis submitted by Robert B. Garland to the Massachusetts Institute of Technology, 1957, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) National Science Foundation Fellow, 1953-1955; William S. Knudsen Fellow, 1955–1956.

(3) A. J. Birch, *J. Chem. Soc.*, 367 (1950); C. Djerassi, L. Miramontes, G. Rosenkranz and F. Sondheimer, THIS JOURNAL, **76**, 4092 (1954); A. Sandoval, G. H. Thomas, C. Djerassi, G. Rosenkranz and F. Sondheimer, *ibid.*, **77**, 148 (1955); A. Zaffaroni, H. J. Ringold, G. Rosenkranz, F. Sondheimer, G. H. Thomas and C. Djerassi, *ibid.*, **76**, 6210 (1954); P. D. Meister, U. S. Patent 2,678,933, May 18, 1954 [*C. A.*, **49**, 6326 (1955)]; H. J. Ringold, G. Rosenkranz and F. Sondheimer, THIS JOURNAL, **78**, 2477 (1956); C. Djerassi, A. E. Lippman and J. Grossman, *ibid.*, **78**, 2479 (1956); J. A. Hartman, A. J. Tomasewski and A. S. Dreiding, *ibid.*, **78**, 5662 (1956); F. B. Colton, L. N. Nysted, B. Riegel and A. L. Raymond, *ibid.*, **79**, 1123 (1957).

(4) C. Djerassi, L. Miramontes and G. Rosenkranz, *ibid.*, **75**, 4440 (1953).

(5) A. L. Wilds and N. A. Nelson, *ibid.*, **75**, 5366 (1953).



higher activity than the corresponding C-10 methyl compounds. Removal of the C-19 methyl group of progesterone leads to an increase in biological activity of four to eight times.[4] It is of considerable interest, therefore, to make available the 18,19-dinor analog of progesterone for testing to help determine the importance of the C-18 methyl group for biological activity. This paper describes the preparation of 18,19-dinorprogesterone (XVIIb) and 14α-hydroxy-18,19-dinorprogesterone (XVIIa).

14-Hydroxy-18,19-dinorprogesterone.—As the starting material in our work, 1-keto-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene (I) was prepared from 2-methoxynaphthalene by methods described in the literature.[6] Catalytic reduction of I with a palladium-on-charcoal catalyst appeared, on the basis of infrared and ultraviolet spectra, to yield only 7-methoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene. The ketone was reduced to II in 90% yield by lithium in liquid ammonia.

(6) G. Stork, THIS JOURNAL, **69**, 576 (1947); V. C. E. Burnop, G. H. Elliott and R. P. Linstead, *J. Chem. Soc.*, 727 (1940); E. Schwenk and D. Papa, THIS JOURNAL, **67**, 1432 (1945); G. Stork, *ibid.*, **69**, 2936 (1947); F. J. Villani, M. S. King and D. Papa, *J. Org. Chem.*, **18**, 1578 (1953).

The sequence of reactions for attaching ring D on the ketone II is based upon the method of Sarett and co-workers for their synthesis of cortisone.[7] The first problem involved the introduction of a methallyl group in the 2-position of 1-keto-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene (II). It was found that this transformation could be accomplished by way of the hydroxymethylene derivative III which was obtained in 68% yield. The sodium salt of III reacted readily with methallyl iodide in N,N-dimethylformamide solution. A short treatment of the crude product with potassium hydroxide and chromatographic purification gave 1-keto-2α-methallyl-7-methoxy-1,2,3,4,4aα-9,10,10aβ-octahydrophenanthrene (IV) in 39% yield. In a previous attempt a suspension of the sodium salt in benzene did not react with methallyl iodide to any appreciable extent after 24 hours. It was subsequently found that the over-all yield in going from I to IV could be improved by altering the sequence of reactions. The unsaturated ketone I was first alkylated *via* the hydroxymethylene derivative V, which was formed in 90% yield, to form 1-keto-2-methallyl-1,2,3,4,9,10-hexahydrophenanthrene (VI) in 69% yield. This material was then reduced using a solution of lithium in ammonia to give IV in 65% yield. By using this latter method the over-all yield of IV from I was increased from 24 to 41%.

The ketone IV was treated with ethoxyacetylenemagnesium bromide and the crude mixture of ethoxyethinylcarbinols was hydrated by a dilute aqueous solution of sulfuric acid in tetrahydrofuran. The major product of this reaction was not the unsaturated ester VIIa but rather the β-hydroxy ester VIIIa.[8] When the crude product was hydrolyzed the only material obtained (43%) was the β-hydroxy acid VIIIb. Dehydration of this material VIIIb *via* the methyl ester using thionyl chloride in pyridine produces an unconjugated unsaturated acid IXa. This acid was shown to be unconjugated by both physical and chemical evidence. The extinction coefficient of the acid at 220 mμ (ϵ 12,950) is largely accounted for by the absorption of the aromatic ring. If the double bond were conjugated with the carboxyl group, the extinction coefficient should be about 21,000, corresponding to the summation of the extinction coefficients for the aromatic ring (*ca.* 11,000) and a trisubstituted conjugated unsaturated acid (*ca.* 10,000).[7b] The infrared spectrum of the methyl ester IXb showed an absorption maximum at 5.77 μ which is practically identical with that found in the saturated esters of this series but different from that observed (5.85 μ) for the related conjugated ester VIIa. The acid IXa was recovered unchanged from a solution of lithium in ammonia, these conditions being favorable for the reduction of conjugated unsaturated acids.[7b]

When the crude product, obtained from the reaction of IV with ethoxyacetylenemagnesium bromide followed by sulfuric acid-catalyzed hydration, was chromatographed two bands were obtained. The first of these was an oily mixture of unsaturated esters VIIa, amounting to a 9% yield. This material was used in the preparation of 18,19-dinorprogesterone (XVIIb). The second band contained the major product, which was isolated as the crystalline β-hydroxy ester VIIIa in 79% yield. Dehydration of this material using thionyl chloride in pyridine produced the crystalline β,γ-unsaturated ester IXc related to the unsaturated acid IXa described above. A portion of the unsaturated ester was treated with a dilute sodium ethoxide solution in an effort to isomerize the double bond, but it was recovered unchanged as revealed by infrared and ultraviolet spectra.

The reduction of VIIIa with lithium aluminum hydride gave the 1,3-diol VIIIc. In some runs, notably when the reaction mixture was allowed to become warm, two by-products were also obtained. Both of the by-products gave IV upon oxidation with the chromium trioxide–pyridine complex. Apparently VIIIa underwent a reverse aldol reaction to form IV which was then reduced to the epimeric alcohols[9] corresponding to IV.

Compound VIIIc gave a monotosylate VIIId in 80% yield. The tosylate upon oxidation with an equivalent amount of osmium tetroxide, followed by cleavage of the glycol with periodate and cyclization with base gave 3-methoxy-17-acetyl-18-nor-1,3,5(10)-estratriene-14-ol (Xa) in 19% yield. Two by-products were obtained from this reaction. One of them had the correct analysis for $C_{20}H_{26}O_3$ and showed no infrared bands characteristic of hydroxyl, carbonyl or olefinic groupings. On the basis of the information available, structure XI is tentatively assigned. The second by-product had the correct analysis for $C_{21}H_{34}O_4$ and is believed to be similar in structure to a by-product isolated by Sarett and co-workers from a similar series of reactions.[7c] This by-product gave the lactone XIII when oxidized with the chromium trioxide–pyridine complex, fixing the stereochemistry of the new asymmetric center. The structure of this by-product is therefore designated as XII.

It was found that the yield of Xa could be greatly improved by modifying the conditions of osmium tetroxide oxidation and periodate cleavage. When a catalytic amount of osmium tetroxide (10% of one equivalent) was used with two equivalents of paraperiodic acid[10] none of the by-product XII was obtained. Instead larger amounts of Xa and XI were obtained. The yield of Xa by this method was 32%.

3-Methoxy-17-acetyl-18-nor-1,3,5(10)-estra-

(7) (a) L. H. Sarett, W. F. Johns, R. E. Beyler, R. M. Lukes, G. I. Poos and G. E. Arth, THIS JOURNAL, **75**, 2112 (1953); (b) G. E. Arth, G. I. Poos, R. M. Lukes, F. M. Robinson, W. F. Johns, M. Feurer and L. H. Sarett, *ibid.*, **76**, 1715 (1954); (c) W. F. Johns, R. M. Lukes and L. H. Sarett, *ibid.*, **76**, 5026 (1954).

(8) While there are many examples of such acetylenic carbinols rearranging to conjugated unsaturated esters, it has been shown[7b] that the stereochemistry of the acetylenic carbinol can influence the formation of products.

(9) The isomer with m.p. 168–169° was formed in lower yield and was oxidized less easily than the isomer with m.p. 93–94°. These results suggest that the high melting isomer is the equatorial alcohol and the low melting isomer, the axial alcohol. See W. G. Dauben, E. J. Blanz, Jr., J. Jiu and R. A. Micheli, THIS JOURNAL, **78**, 3752 (1956), for a discussion of the formation of isomers in lithium aluminum hydride reductions and reference 11 for a comparison of the ease of oxidation of axial and equatorial alcohols.

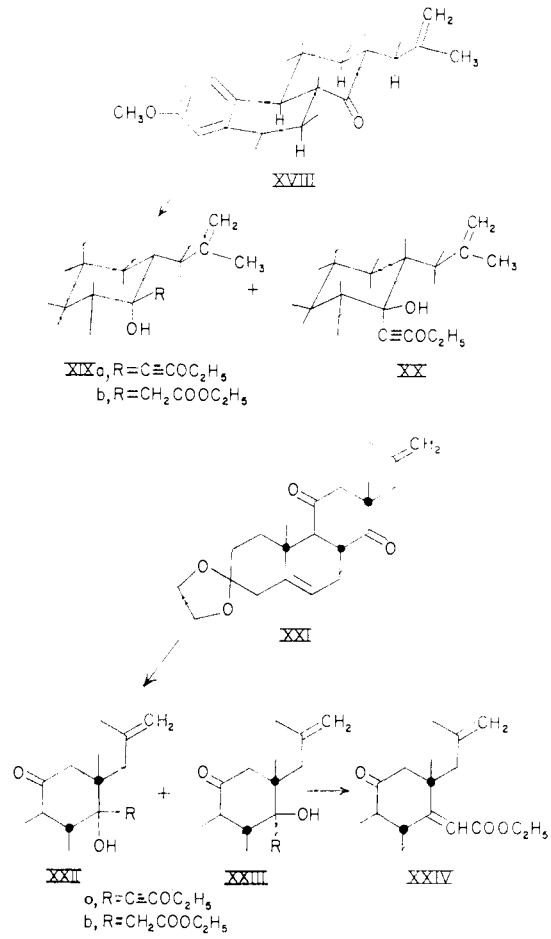
(10) R. Pappo, D. S. Allen, Jr., R. U. Lemieux and W. S. Johnson, *J. Org. Chem.*, **21**, 478 (1956), have described the oxidative cleavage of several olefins by this method.

triene-14-ol (Xa) was reduced with lithium and alcohol in ammonia.[5] The crude product XIVa was hydrolyzed with oxalic acid to XV, which was not isolated as such. Isomerization with sodium ethoxide to XVI and oxidation with the chromium trioxide–pyridine complex gave 14-hydroxy-18,19-dinorprogesterone (XVIIa). The intermediate stages in the conversion of Xa to XVIIa were identified only on the basis of the infrared spectra.

Configuration of 14-Hydroxy-18,19-dinorprogesterone.—The concepts of conformational analysis[11] would lead one to predict that the most stable conformation of a compound such as IV would be the one having a *trans* ring junction and an equatorial configuration of the bulky methallyl side chain. Equilibration of other stereochemical isomers of IV with base should result in their isomerization through enolization to this conformation. Compound IV was subjected to an equilibration with methanolic sodium methoxide. The crystalline ketone, isolated in good yield is, therefore, assigned the conformation shown either in IV or XVIII.[12]

In the work aimed at the synthesis of cortisone, the ketone XXI gave two ethoxyethinylcarbinols.[7b] The major product, obtained in 76% yield, was assigned structure XXIIIa, while the minor product, obtained in 10% yield, was assigned structure XXIIa. When these two materials were treated with dilute sulfuric acid in tetrahydrofuran, XXIIa produced only a β-hydroxy ester XXIIb. On the other hand, XXIIIa gave a mixture from which a 45% yield of an unsaturated ester XXIV and a 28% yield of a β-hydroxy ester XXIIIb were obtained. When XXIIIb was dehydrated with thionyl chloride in pyridine a 75% yield of XXIV was obtained. When XXIIb was similarly dehydrated, an amorphous material was obtained which apparently contained only a small amount of XXIV.

A similar series of reactions was carried out in the present work. In the reaction of XVIII with ethoxyacetylene magnesium bromide a new asymmetric center is produced. By inspection of formula XVIII it can be seen that the approach of the Grignard reagent to the carbonyl group is relatively unhindered from the topside of the molecule, but that three β-axial hydrogen atoms and part of the methallyl side chain shield the carbonyl group from a bottom-side attack. The configuration of the major product in this reaction would therefore be XIXa rather than structure XX.[13] By analogy to the reactions of the acetylenic carbinols XXIIa and XXIIIa, if the major product in our work is in reality XIXa, treatment with dilute sulfuric acid should yield a β-hydroxy ester rather than an α,β-unsaturated ester. As expected, this reaction gave a preponderance (79%) of the β-hydroxy ester XIXb and only 9% of a crude unsaturated ester (VIIa) (presumably derived from XX). The properties of the hydroxy ester are consistent with its structure. Dehydration of XIXb gave as the only product a β,γ-unsaturated ester IXc. In view of these considerations, the β-hydroxy ester has been assigned the configuration indicated, namely, 1-carbethoxymethyl - 2α - methallyl - 7 - methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthren-1α-ol (VIIIa; corresponds to XIXb).



With the cyclization of ring D, the fifth asymmetric center is introduced. The fused five-membered ring is non-planar, and from an inspection of molecular models it is apparent that a 17β-substituent would have what corresponds to an equatorial configuration rather than a less stable axial configuration.[11] Consequently, the equilibration of a 17-acetyl steroid with acid or base should result in an equilibrium mixture containing chiefly the compound with a 17β-substituent. Such examples can be found in the normal steroid series.[14] In the cyclization step, compound Xa was subjected to prolonged treatment with base. Under these conditions equilibration should have occurred to give chiefly the 17β-substituted compound. It is also felt that the last asymmetric center (C-10 hydrogen atom of XVIIa) is in the stable β-con-

(11) D. H. R. Barton, *Experientia*, **6**, 316 (1950).

(12) All of the compounds in this paper having asymmetric centers are racemates. For convenience, the structure of only one of the *di*-forms is shown in each case.

(13) This is in contrast to the work of Sarett and co-workers who found that the major ethoxyethinylcarbinol XXIII from XXI has the opposite configuration at the carbinol carbon atom. In their case the adjacent axial methyl group must shield the carbonyl group from a preferential topside attack. The 4-keto group may also exert an influence in determining the orientation of the product.

(14) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed., Reinhold Publ. Corp., New York, N. Y., 1949, p. 390.

figuration by analogy with all of the other cases of Birch reductions of ring A aromatic steroids.[5,15]

18,19-Dinorprogesterone.—As was noted above in the discussion of the preparation of the β-hydroxy ester VIIIa, a small amount of an unsaturated ester fraction was obtained. In one experiment a crystalline *cis* or *trans* ester VIIa was obtained from this fraction. It was found that either the oily mixture of unsaturated esters or the crystalline ester could be used for the preparation of 18,19-dinorprogesterone (XVIIb).

Saponification of the unsaturated ester mixture gave a non-crystalline mixture of acids which was treated with a solution of lithium in liquid ammonia. Conversion of the reduced material with diazomethane gave a crystalline ester VIIIe. When these same reactions were carried out with crystalline VIIa, the over-all conversion to VIIIe was 50% (the other possible isomer was not obtained). The carbomethoxymethyl side chain at the newly introduced asymmetric carbon atom is believed to have the equatorial or β-configuration. This assignment of configuration is based only on analogy with similar reductions where it has been shown that the thermodynamically stable isomer is formed.[16] For example, the lithium in liquid ammonia reduction of $\Delta^{1,9}$-2-octalone gives *trans*-β-decalone of 90% purity.[17] In this reduction the addition of the proton β to the carbonyl group occurs from the sterically hindered side of the molecule (3 β-axial hydrogen atoms) to give the thermodynamically more stable *trans*-isomer.

The ester VIIIe was reduced with lithium aluminum hydride to the corresponding alcohol which was converted to the tosylate VIIIf. The tosylate was subjected to oxidation by a mixture of paraperiodic acid and a catalytic amount of osmium tetroxide[10] followed by treatment with sodium methoxide to give 3-methoxy-17-acetyl-18-nor-1,3,5(10)-estratriene (Xb) as the only product isolated. This tetracyclic compound was reduced with lithium and alcohol in liquid ammonia, the crude product was hydrolyzed with acid, and then oxidized with chromic acid to give 18,19-dinorprogesterone (XVIIb). The 17-acetyl group and the C-10 hydrogen atom of XVIIb are believed to have the stable β-configuration for the same reasons expressed above in assigning these configurations to the 14-hydroxy derivative XVIIa.

Experimental[18]

1-Keto-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene (II).—A solution of 1.08 g. (0.154 mole) of lithium in 1 l. of anhydrous liquid ammonia was prepared in a flask equipped with a stirrer, dropping funnel and a Dry Ice-cooled condenser protected from the atmosphere with a soda lime tube. A solution of 16 g. (0.07 mole) of 1-keto-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene (I) (prepared from 2 methoxynaphthalene)[6] in 500 ml. of dry ether was added as rapidly as possible. The mixture was stirred for 30 minutes at which time 20 g. of solid ammonium chloride was added. The ammonia and ether were allowed to evaporate to dryness, 500 ml. of water was added and the mixture was extracted with ether. The ether extract was washed with water and dried. Distillation of the ether left 15.5 g. of material which after chromatographic purification on Alcoa Grade F-20 Alumina gave 14.5 g. (90%) of white crystals, m.p. 97–100°. This material appeared to be free of impurities other than the *cis* ketone[16] and could be used directly in subsequent reactions. Recrystallization from dilute methanol raised the melting point to 105–107°. A further recrystallization from hexane gave VII as needles, m.p. 109–109.5° (lit.[19,20] m.p. 109°, 107–108°, 103.5–106°).

Catalytic Reduction of 1-Keto-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene (I).—A solution of 0.525 g. of the ketone in 12 ml. of ethanol and 1 drop of acetic acid was hydrogenated in the presence of 0.15 g. of a 30% palladium-on-charcoal catalyst. The hydrogen uptake stopped after 50 minutes at which time the catalyst was removed by filtration and the solvent was distilled to leave 0.40 g. (75%) of a colorless oil, λ_{max}^{EtOH} 225 (ε 12,550), 277 (ε 2,760) and 286 mμ (ε 2,360). The infrared spectrum shows none of the characteristic bands for hydroxyl, carbonyl or olefinic groupings. These data indicate that the product is 7-methoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene.

1-Keto-2-methallyl-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene (VI).—N,N-Dimethylformamide (100 ml.) was added with stirring to a mixture of 34 g. of 1-keto-2-hydroxymethylene-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene (V)[21] and 3.3 g. of sodium hydride under a nitrogen atmosphere. After 30 minutes the flask was cooled in an ice-bath while 30 g. of methallyl iodide was added. After 1 hour at room temperature most of the solvent was removed by distillation under reduced pressure. A solution of 10 g. of potassium hydroxide in 25 ml. of water was added and the solution was stirred for 30 minutes at which time it was diluted with water and extracted with ether (2 × 500 ml.). The ether extract was washed with water, dried and concentrated to give a residue (35.9 g.), which was chromatographed on 600 g. of Alcoa Grade F-20 Alumina. The product was eluted with benzene to yield 28.6 g. which after crystallization from methanol gave 25.8 g. (69%) of white crystals, m.p. 61–62°. Further recrystallization produced an analytical sample of VI melting at 61.8–62.6°.

Anal. Calcd. for $C_{19}H_{22}O_2$: C, 80.82; H, 7.86. Found: C, 80.82; H, 8.03.

1-Keto-2α-methallyl-7-methoxy-1,2,3,4aα,9,10,10aβ-octahydrophenanthrene (IV). (A) From 1-Keto-2-hydroxymethylene-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene (III).—A solution of 5.16 g. of III[21] and 2 drops of ethanol in 40 ml. of redistilled N,N-dimethylformamide was added to 0.53 g. of sodium hydride under a nitrogen atmosphere. The mixture was stirred for 1 hour and then 5.46 g. of methallyl iodide was added and stirring was continued for 1 hour more. A solution of 1.68 g. of potassium hydroxide in 1 ml. of water and 5 ml. of methanol was added and stirring was continued for 30 minutes at which time 300 ml. of water was added and the material was extracted with ether. Acidification of the aqueous solution yielded 0.91 g. of III, m.p. 132–136°. The ether extract was washed with water, dried and concentrated to give 4.4 g. of a semi-crystalline residue which was chromatographed on Alcoa Grade F-20 alumina. The first material eluted was oily but the fractions which crystallized readily upon seeding were combined and recrystallized from methanol to give 1.82 g. (32% conversion, 39% yield) of 1-keto-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene (IV), m.p. 104–105°. Further recrystallization raised the melting point to 106.2–106.6°.

Anal. Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.22; H, 8.64.

(B) From 1-Keto-2-methallyl-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene (VI).—A solution of 25.8 g. of VI in 200 ml. of ether was added to a solution of 1.75 g. of lithium in 500 ml. of anhydrous liquid ammonia. After the

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(17) E. E. van Tamelen and W. C. Proost, Jr., THIS JOURNAL, **76**, 3632 (1954).

(18) Melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses. The infrared spectra were determined with a Baird or Perkin-Elmer (model 21) spectrophotometer fitted with a sodium chloride prism. Ultraviolet spectra were determined in 95% ethanol with a Cary recording spectrophotometer (model 11MS).

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(21) W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg and L. J. Chinn, *ibid.*, **74**, 2832 (1952).

mixture had been stirred for 15 minutes, a small amount of ethyl acetate was added to destroy the excess lithium and then 30 g. of solid ammonium chloride was added. After the ammonia and ether had evaporated, 500 ml. of water and 500 ml. of ether were added and the aqueous layer was extracted with ether. The ether layers were washed successively with water, 2% hydrochloric acid solution, water and saturated sodium chloride solution. The dried ether solution was evaporated and the residue (26 g.) was dissolved in 50 ml. of absolute methanol. A solution of sodium methoxide prepared from 150 mg. of sodium and 50 ml. of methanol was added and the mixture was kept at room temperature for 3 hours during which time a bulky mass of crystals formed. After the addition of 1 ml. of acetic acid the mixture was cooled to 0° and filtered. The solid product was washed well with aqueous methanol and recrystallized from methanol to yield 13 g., m.p. 104.5–105.5°. After concentration of the filtrates and chromatographic purification an additional 3.8 g., m.p. 105–106°, was obtained. The total yield of IV was 16.8 g. (65%). A mixed melting point with the analytical sample prepared by method A showed no depression.

1-Carboxymethyl-2α-methallyl-7-methoxy-1,2,3,4,4aα,-9,10,10aβ-octahydrophenanthrene-1α-ol (VIIIb).—A solution of 0.994 g. of ethoxyacetylene[22] and 6 ml. of ether was added to a solution of ethylmagnesium bromide prepared from 0.338 g. of magnesium turnings, 1.05 ml. of ethyl bromide and 13.5 ml. of ether. The mixture was refluxed for 2 hours during which time a brown oil separated. The oil was dissolved by the addition of 10 ml. of anhydrous benzene. The solution was cooled in an ice-bath while 2.00 g. of 1-keto-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene (IV) in 8 ml. of benzene was added. The mixture was stirred at room temperature for 3 hours, refluxed for 1 hour and cooled in an ice-bath before adding 50 ml. of ice-water. The aqueous layer was extracted with ether; ammonium chloride was added as needed to break up emulsions. The organic layers were combined, washed with water and dried. The solvents were distilled under reduced pressure and a mixture of 1.4 ml. of 10% (w./v.) sulfuric acid in 23 ml. of tetrahydrofuran was added to the residue with cooling in an ice-bath. The mixture was stirred at room temperature for 3 hours when 10.5 ml. of 0.5 *N* sodium bicarbonate solution was added. The crude hydroxy ester VIIIa was extracted with ether and the organic layer was washed with water and concentrated *in vacuo*. The residue was heated under reflux for 3 hours with a solution of 6.1 g. of potassium carbonate and 0.5 g. of potassium hydroxide in 45 ml. of water and 45 ml. of methanol. The methanol was removed by distillation and 100 ml. of water was added. The solution was washed with ether, acidified with saturated sodium dihydrogen phosphate solution and the product was then extracted with ether. The ether extract was washed with water, dried and concentrated to give a residue which was crystallized from dilute methanol to yield 1.2 g. (43%) of VIIIb, m.p. 145–149°. Further recrystallizations yielded a sample melting at 150.4–151.2°, λ_{max}^{KBr} 3.0, 5.92 and 11.2 μ.

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19. Found: C, 73.14; H, 8.41.

Unsaturated Acid (IXa).—1-Carboxymethyl-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene-1α-ol (VIIIb) (670 mg.) was converted to the methyl ester with diazomethane. The crude methyl ester (700 mg.) was dissolved in 7 ml. of pyridine, cooled and treated with a solution of 0.4 ml. of thionyl chloride and 2 ml. of pyridine for 10 minutes. The reaction mixture was poured onto a mixture of 4 g. of sodium bicarbonate and 40 ml. of ice-water and then extracted with hexane. The hexane extract was concentrated *in vacuo* and the residue chromatographed on Merck acid-washed alumina. The first band (490 mg.), which was eluted with hexane–benzene (1:1), was hydrolyzed by refluxing it with a mixture of 1.5 g. of potassium carbonate, 15 ml. of water and 20 ml. of methanol for 6 hours. The methanol was removed by distillation and 50 ml. of water was added. The aqueous solution was washed with ether and acidified with sodium dihydrogen phosphate to give 220 mg. (33%) of material, m.p. 162–168°. Several recrystallizations from benzene gave an analytical sample of IXa, m.p. 190–191°, λ_{max}^{KBr} 5.92 and 11.25 μ, λ_{max}^{EtOH} 278.5 (ε 2,540) and 287 mμ (ε 2,320) with an inflection at 220 mμ (ε 12,950). These data indicate that the carboxyl group is not conjugated with the carbon–carbon double bond.

Anal. Calcd. for $C_{21}H_{26}O_3$: C, 77.28; H, 8.03. Found: C, 77.55; H, 8.18.

A solution of 200 mg. of the acid in tetrahydrofuran solution was treated with an excess of ethereal diazomethane to form 140 mg. (67%) of the methyl ester IXb, m.p. 75–76°. Further recrystallizations from methanol gave a sample which melted at 76.0–76.6°, $\lambda_{max}^{CCl_4}$ 5.77 and 11.2 μ.

Anal. Calcd. for $C_{22}H_{28}O_3$: C, 77.60; H, 8.29. Found: C, 77.46; H, 8.32.

1-Carbethoxymethyl-2α-methallyl-7-methoxy-1,2,3,4,-4aα,9,10,10aβ-octahydrophenanthrene-1α-ol (VIIIa).—This compound has been described above as an intermediate in the preparation of the corresponding acid VIIIb. Using the procedure described above with 0.356 g. of magnesium turnings, 1.61 g. of ethyl bromide, 1.05 g. of ethoxyacetylene and 2.00 g. of IV and about the same quantities of solvents, there was obtained after treatment with dilute sulfuric acid 2.7 g. of crude product which was chromatographed on 125 g. of Merck acid-washed alumina. The first band of material eluted using hexane–benzene (4:1) amounted to 180 mg. (9%) and was a crude unsaturated ester (VIIa) as indicated by the infrared spectrum, $\lambda_{max}^{CCl_4}$ 5.85 μ. The second band eluted using benzene–ether (49:1) amounted to 2.5 g. which upon crystallization from about 5 ml. of hexane gave 2.06 g. (79%) of the product VIIIa, m.p. 67.5–68°. Further recrystallizations from aqueous methanol produced an analytical sample which melted at 68.2–68.8°, $\lambda_{max}^{CCl_4}$ 2.86, 5.78 and 11.2 μ (a shoulder at 5.85 μ may be due to hydrogen-bonded carbonyl).

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 73.83; H, 8.79.

In one run the first portion of the unsaturated ester fraction crystallized to yield 30 mg. of VIIa, m.p. 90-91° after recrystallization from methanol, λ_{max}^{KBr} 5.83 μ.

Dehydration of 1-Carbethoxymethyl-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene-1α-ol (VIIIa).—A solution of 2.25 g. of the β-hydroxy ester in 25 ml. of dry pyridine was cooled to 10° and a solution of 1.5 ml. of thionyl chloride in 5 ml. of pyridine was added with stirring. The mixture was allowed to stand for 10 minutes and then was poured onto 18 g. of sodium bicarbonate in 180 ml. of ice-water. The mixture was extracted with hexane. The hexane extract was washed once with water and the solvent was removed by distillation. The residue (2.2 g.) was crystallized from 5 ml. of methanol to yield 1.63 g. (76%) of the product, m.p. 57.5–59°. After further recrystallizations a sample was obtained which melted at 59.2–60.0°, $\lambda_{max}^{CCl_4}$ 5.77 (unconj. ester) and 11.2 μ, λ_{max}^{EtOH} 278 (ε 2,280) and 286.5 mμ (ε 1,920) as well as an inflection at 220 mμ (ε 12,900). These data suggest structure IXc.

Anal. Calcd. for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 77.64; H, 8.45.

When 177 mg. of this ester was treated with a sodium ethoxide solution from 10 mg. of sodium and 5 ml. of absolute ethanol at room temperature overnight, 130 mg. of crude material was recovered. The infrared spectrum of this crude product is identical with that of the starting material. The ultraviolet spectrum showed maxima at 277.5 (ε 2,290) and 286 mμ (ε 1,890) and an inflection at 220 mμ (ε 11,200). Thus there seems to have been no isomerization to an α,β-unsaturated ester.

1-(2-Hydroxyethyl)-2α-methallyl-7-methoxy-1,2,3,4,4aα,-9,10,10aβ-octahydrophenanthrene-1α-ol (VIIIc).—A solution of 3.95 g. of 1-carbethoxymethyl-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene-1α-ol (VIIIa) in 75 ml. of anhydrous ether was cooled in an ice-bath while 20 ml. of a 1 *M* ethereal solution of lithium aluminum hydride was added cautiously with stirring. The mixture was stirred at room temperature overnight and then the excess reducing agent was destroyed by the addition of 5 ml. of ethyl acetate followed by 5 ml. of water. The mixture was filtered through Super-cel and the filter cake was washed with 100 ml. of chloroform. The combined solvents were distilled under reduced pressure and the residue (4 g.) was crystallized from benzene–hexane to yield in two crops 3.0 g. (86%), m.p. 96–98°. After recrystallization from aqueous methanol, 2.5 g. of material melting at 108–110°

(22) E. A. Braude and O. H. Wheeler, *J. Chem. Soc.*, 320 (1955).

was obtained. Further recrystallizations from aqueous methanol gave an analytical sample of VIIIc which melted at 109.6–110.2°.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.33; H, 9.15. Found: C, 76.16; H, 9.15.

In another run, in which solid lithium aluminum hydride was added to a solution of 2 g. of VIIIa in tetrahydrofuran (the reaction became warm enough for mild boiling), two by-products were obtained. The first crystallized readily from aqueous methanol to give 0.30 g. (19%), m.p. 168–169°. The analytical sample melted at 169.0–170.0°, $\lambda_{max}^{CHCl_3}$ 2.81 μ.

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.67; H, 9.15. Found: C, 79.91; H, 9.21.

After the reaction of 200 mg. of this material with the chromium trioxide–pyridine complex[23] and chromatographic separation, 40 mg. (m.p. 168–169°) was recovered unchanged. The other product isolated (60 mg., 30%, m.p. 105–106°) was shown to be identical with IV when a mixed melting point was not depressed.

The filtrates from the crystallization of the first by-product were concentrated and the residue (1.6 g.) was chromatographed on 60 g. of Merck reagent alumina. The first material eluted with benzene–ether (9:1) gave 0.54 g. (35%) of a solid, m.p. 93–94°, after crystallization from aqueous methanol. The analytical sample melted at 93.0–93.8°, $\lambda_{max}^{CHCl_3}$ 2.82 μ.

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.67; H, 9.15. Found: C, 79.52; H, 9.01.

Oxidation of 340 mg. of this material with the chromium trioxide–pyridine complex[23] and crystallization of the product from methanol gave 240 mg. (71%) of IV, m.p. 105–106°.

Further elution with ether produced a second band which on crystallization from benzene–hexane gave 0.69 g. (39%) of the diol VIIIc, m.p. 104–106°.

1-(2-Tosyloxyethyl)-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene-1α-ol (VIIId).—A solution of 1.8 g. of *p*-toluenesulfonyl chloride in 10 ml. of dry benzene was added to a solution of 2.6 g. of 1-(2-hydroxyethyl)-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene-1α-ol (VIIIc) in 10 ml. of dry pyridine which was cooled in an ice-bath. The mixture was stored at 0° for 21 hours at which time 60 ml. of 5% sodium bicarbonate solution was added and the mixture was stirred at 0° for 15 minutes. The mixture was extracted with ether and the ether extract was washed with water and dried. The solvents were removed *in vacuo* and the residue was crystallized from benzene–hexane to yield in two crops 3.05 g. (80%) of the tosylate VIIId, m.p. 120–122°. After further recrystallizations the analytical sample melted at 116–117° dec. (The material from the first crystallization contained a trace of pyridine which apparently acted as a stabilizing agent.)

Anal. Calcd. for $C_{28}H_{36}O_5S$: C, 69.39; H, 7.49; S, 6.62. Found: C, 69.57; H, 7.51; S, 6.69.

3-Methoxy-17-acetyl-18-nor-1,3,5(10)-estratriene-14-ol (Xa).—A solution of 60 mg. of osmium tetroxide in 1.2 ml. of tetrahydrofuran (distilled from sodium) was added to a solution of 750 mg. of 1-(2-tosyloxyethyl)-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene-1α-ol (VIIId) in 15 ml. of tetrahydrofuran and 2 ml. of pyridine. After the solution had been stirred for 10 minutes a solution of 820 mg. of paraperiodic acid in 5 ml. of water was added. The mixture was stirred for 10 hours at room temperature and was then cooled in an ice-bath while a solution of 3 g. of sodium sulfite in 20 ml. of water was added. The mixture was stirred for 30 minutes and then extracted with ether. The ether extract was washed with water and dried. The solvents were removed *in vacuo* and the residue (750 mg.) was dissolved in 10 ml. of anhydrous *t*-butyl alcohol and added to 30 ml. of 0.112 *N* potassium *t*-butoxide in *t*-butyl alcohol. The mixture was stored at room temperature overnight. After the mixture had been diluted by the addition of 100 ml. of water, it was extracted with chloroform and the extracts were washed with water and dried. The solvents were distilled *in vacuo* and the residue (550 mg.) was chromatographed on 75 g. of Merck reagent alumina. After the elution of 110 mg. of a by-product with benzene–ether (9:1) (see below), the product (190 mg.) was eluted with ether. Crystallization from benzene–hexane gave 154 mg. (32%) of Xa, m.p. 130–132°. Further recrystallizations yielded an analytical sample which melted at 131.2–132.0°, λ_{max}^{KBr} 2.84, 5.92 and 6.20 μ.

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.53; H, 8.64.

The first fraction from the chromatogram (above) was crystallized from aqueous methanol to give 83 mg. (17%) of a by-product XI, m.p. 126–127°. The analytical sample melted at 127.2–127.8°.

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.08; H, 8.20.

The infrared spectrum shows no bands characteristic of hydroxyl or carbonyl groupings. On the basis of this evidence this by-product was assigned the structure of the ketal XI.

In other runs in which the methylene group was oxidized in a stepwise fashion[7c] first by osmium tetroxide and then by paraperiodic acid these same two products were obtained together with a second by-product, which was eluted from the alumina by ether–methanol (19:1). In a run involving 1.5 g. of VIIId the yield of 3-methoxy-17-acetyl-1,3,5,(10)-estratriene-14-ol (Xa) was 190 mg. (19%) while the yield of the ketal XI was 110 mg. (11%). The polar by-product (XII) was crystallized from benzene–hexane and amounted to 250 mg. (23%), m.p. 186–187°. The analytical sample melted at 187–187.5°, λ_{max}^{KBr} 2.86 μ.

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.81; H, 8.73. Found: C, 72.62; H, 8.74.

14-Hydroxy-18,19-dinorprogesterone (XVIIa).—A solution of 200 mg. of Xa in 10 ml. of absolute ethanol and 50 ml. of ether was added dropwise over 10 minutes to a solution of 840 mg. of lithium in 250 ml. of anhydrous ammonia. This addition was followed immediately by an additional 8 ml. of ethanol. When the blue color had disappeared, 10 ml. of water was added and the ammonia was allowed to evaporate. After the addition of 50 ml. of water the mixture was extracted with chloroform. The extract was washed with water, dried and the chloroform was then removed *in vacuo* to give 200 mg. of the crude enol ether XIVa, $\lambda_{max}^{CHCl_3}$ 2.79 and 2.92 μ (OH), 5.86 and 6.01 μ (unconj. enol ether[5]).

The enol ether was dissolved in 30 ml. of methanol. A solution of 0.6 g. of oxalic acid dihydrate in 6 ml. of water was added and the mixture was allowed to stand at room temperature for 2 hours. The mixture was diluted by the addition of 50 ml. of saturated sodium bicarbonate solution and was extracted with chloroform. The extracts were washed with water, dried and concentrated *in vacuo* to leave 220 mg. of the crude β,γ-unsaturated ketone XV, $\lambda_{max}^{CHCl_3}$ 2.79 and 2.92 μ (OH) and 5.87 μ (unconj. CO).

The crude ketone was dissolved in 10 ml. of absolute ethanol and a sodium ethoxide solution from 20 mg. of sodium in 5 ml. of ethanol was added. The mixture was kept at 50° under a nitrogen atmosphere for 10 minutes. The mixture was then acidified with a few drops of acetic acid. After dilution with water the mixture was extracted with chloroform. The extract was washed with water, dried and concentrated to leave 230 mg. of the crude α,β-unsaturated ketone XVI. This material was dissolved in 2 ml. of pyridine and added to a suspension from 250 mg. of chromium trioxide in 3 ml. of pyridine. The mixture was stirred at room temperature overnight, then 5 ml. of water and 50 ml. of chloroform was added. The mixture was filtered through Super-Cel and the filter cake was washed with additional chloroform. The extracts were washed with water, dried and concentrated *in vacuo* to leave a residue of 200 mg. Upon chromatographic purification of this residue on 40 g. of Merck acid-washed alumina, the product, which was eluted with ether, amounted to 80 mg. Crystallization from benzene–hexane gave 65 mg., m.p. 145–148°. Recrystallization of this sample from aqueous methanol gave 42 mg. (22%) of XVIIa, m.p. 160–161°. An analytical sample crystallized from benzene–hexane melted at 161.4–162.0°, λ_{max}^{KBr} 2.89, 5.85, 6.02 and 6.18 μ.

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.37; H, 8.44.

1,2-(3'-Oxa-4'β-methyl-4'-carboxycycloheptano)-7-methoxy-1,2β,3,4,4aα,9,10,10aβ-octahydrophenanthrene-1α-ol

(23) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, 75, 422 (1953).

Lactone (XIII).—A solution of 330 mg. of XII in 5 ml. of pyridine was added to a suspension from 0.75 g. of chromium trioxide and 7.5 ml. of pyridine. The mixture was allowed to stand at room temperature overnight and was then diluted with 50 ml. of water. The resulting mixture was extracted with ether and the ether extract was washed with water, dilute sodium hydroxide solution and dried. The solvents were removed *in vacuo* and the residue (270 mg.) was chromatographed on 12 g. of Merck acid-washed alumina. The first band, eluted with benzene and amounting to 230 mg. was crystallized from benzene–hexane to give 190 mg. (59%) of XIII, m.p. 203–204°. The analytical sample melted at 203.2–203.6°, λ_{max}^{KBr} 5.73 μ.

Anal. Calcd. for $C_{21}H_{26}O_4$: C, 73.67; H, 7.66. Found: C, 73.94; H, 7.78.

1β-Carbomethoxymethyl-2α-methallyl-7-methoxy-1,2,3,4,4aα,9,10,10aβ-octahydrophenanthrene (VIIIe).—A solution of 0.2 g. of potassium hydroxide and 2.0 g. of potassium carbonate in 5 ml. of water was added to a solution of 0.95 g. of the crude unsaturated ester VIIa (see preparation of VIIIa above for the source of this material) in 15 ml. of methanol. The mixture was refluxed for 4 hours and then diluted with 10 ml. of water. The methanol was removed by distillation and the mixture was diluted with 25 ml. of water. After the aqueous solution had been washed with ether it was acidified with a saturated sodium dihydrogen phosphate solution and extracted with chloroform. The chloroform extracts were washed with water, dried and concentrated *in vacuo* to give 0.85 g. of crude unsaturated acid. To a solution of the acid in 5 ml. of dry tetrahydrofuran was added 100 ml. of anhydrous liquid ammonia followed by 50 mg. of lithium with stirring. After 2 hours the excess lithium was destroyed by the addition of 0.5 ml. of ethyl acetate. When the ammonia had evaporated, the product was dissolved in water and the water solution was washed with ether before being acidified with saturated sodium dihydrogen phosphate solution. The product was extracted with chloroform and the extract was washed with water, dried and concentrated *in vacuo*. The residue (0.75 g.) was dissolved in ether. An excess of ethereal diazomethane was added at 0°, and after 1 minute a few drops of acetic acid was added to destroy the excess diazomethane. The solvents were removed *in vacuo* and the residue (0.65 g.) was chromatographed on 2.5 g. of Merck acid-washed alumina. The product (350 mg.) was eluted with hexane–benzene (4:1). Crystallization of this material from methanol gave 183 mg. (20%) of VIIIe, m.p. 100–101°. The analytical sample melted at 103–103.5°, λ_{max}^{KBr} 5.83 and 11.28 μ.

Anal. Calcd. for $C_{22}H_{30}O_3$: C, 77.16; H, 8.83. Found: C, 77.14; H, 8.97.

When the same series of reactions was carried out on 160 mg. of the crystalline ester VIIa, m.p. 90–91°, the over-all yield of VIIIe was 78 mg. (50%), m.p. 101–102°. In this run the intermediate acid VIIb was also obtained as a crystalline compound, m.p. 175–176°, upon acidification of the basic solution. These two crystalline intermediates VIIa and VIIb were not further purified or characterized except by conversion to VIIIe.

3-Methoxy-17-acetyl-18-nor-1,3,5(10)-estratriene (Xb).—Two milliliters of 1 *M* lithium aluminum hydride in ether was added to a solution of 200 mg. of the ester VIIIe in 20 ml. of dry ether. The resulting mixture was refluxed for 6 hours. After the mixture had cooled 1 ml. of ethanol was added to destroy the excess lithium aluminum hydride, then 0.25 ml. of water was added and the mixture was filtered through Super-Cel. The filter cake was extracted with 100 ml. of chloroform and the combined filtrates were concentrated *in vacuo*. The residue (250 mg.) was dissolved in 2 ml. of dry pyridine and a solution of 400 mg. of *p*-toluenesulfonyl chloride in 2 ml. of pyridine and 2 ml. of benzene was added. The mixture was stored at 0° for 16 hours. The mixture was then added to 10 ml. of 5% sodium bicarbonate solution and after thorough mixing the product was extracted with ether and the extract was then washed with water and dried. The solvents were removed *in vacuo* and the residue (270 mg.) was crystallized from aqueous methanol to yield 195 mg. of the tosylate VIIIf, m.p. 73–75°. This material was dissolved in 10 ml. of tetrahydrofuran (distilled from sodium) and a solution of 12.5 mg. of osmium tetroxide in 0.5 ml. of tetrahydrofuran was added. Then a solution of 228 mg. of paraperiodic acid in 2 ml. of water was added and the mixture was stirred at room temperature for 12 hours. A solution of 1.5 g. of sodium sulfite in 10 ml. of water was added and stirring was continued for 30 minutes. The mixture was extracted with ether and the extract was then washed with water and dried. The solvents were removed *in vacuo* and the residue (180 mg.) was dissolved in 10 ml. of absolute methanol. A sodium methoxide solution from 23 mg. of sodium and 5 ml. of methanol was added and the mixture was allowed to stand at room temperature for 48 hours. The reaction mixture was diluted with 50 ml. of water and then extracted with chloroform. The extracts were washed with water and dried. Distillation of the solvents *in vacuo* left a residue of 160 mg. which was chromatographed on 10 g. of Merck reagent alumina. The product (87 mg.) was eluted with hexane–benzene (1:1). Crystallization from aqueous methanol gave 52 mg. of Xb, m.p. 114–115°. The analytical sample melted at 114.4–114.8°, λ_{max}^{KBr} 5.88 μ.

Anal. Calcd. for $C_{20}H_{26}O_2$: C, 80.48; H, 8.78. Found: C, 80.40; H, 8.76.

18,19-Dinorprogesterone (XVIIb).—A solution of 50 mg. of 3-methoxy-17-acetyl-18-nor-1,3,5,(10)-estratriene (Xb) in 5 ml. of absolute ethanol and 25 ml. of ether was added dropwise (over 5 minutes) with stirring to a solution of 420 mg. of lithium in 125 ml. of liquid ammonia. Immediately following the addition, 4 ml. of ethanol was added. When the blue color had disappeared 10 ml. of water was added cautiously and the ammonia was allowed to evaporate. The residue was diluted with water and extracted with chloroform. The extracts were washed with water and dried. The solvents were removed *in vacuo* and the residue (50 mg.) was dissolved in 5 ml. of methanol. After the addition of 3 ml. of 4 *N* hydrochloric acid to the solution, the mixture was refluxed for 1 hour. The mixture was diluted with 50 ml. of saturated sodium chloride solution and then extracted with chloroform. The extracts were washed with dilute sodium bicarbonate solution, water, dried, and then concentrated *in vacuo* to leave a residue of 50 mg. This residue was dissolved in 3 ml. of acetic acid and a solution of 0.03 g. of chromium trioxide in 0.2 ml. of water and 1 ml. of acetic acid was added. The mixture was allowed to stand at room temperature for 4.5 hours and then 5 ml. of methanol was added and the mixture was concentrated *in vacuo*. The residue was diluted with water and extracted with chloroform. The extracts were washed with water and dried. The chloroform was removed *in vacuo* to leave a residue of 45 mg. which was chromatographed on 5 g. of Merck reagent alumina. The product was eluted with benzene. Crystallization from hexane gave 12 mg., m.p. 122–124°. Further recrystallizations produced a sample of XVIIb which melted at 126.0–126.6°, λ_{max}^{KBr} 5.91, 6.00 and 6.28 μ, λ_{max}^{EtOH} 239.5 mμ (ϵ 15,000).

Anal.[24] Calcd. for $C_{19}H_{26}O_2$: C, 79.67; H, 9.16. Found: C, 79.67; H, 9.13.

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(24) Analysis by W. Manser, Mikrolaboratorium, Eidg. Technische Hochschule, Zurich, Switzerland.