and the extracts were evaporated to dryness *in vacuo*. Trituration of the residue with 95% ethanol afforded 0.66 g of crystals, mp 242–244°. A pure sample was crystallized from methanol: mp 242.5–244°; $[\alpha]D$ +140°; λ_{max} 239 mμ (ε 14,000); $\nu_{max}^{CS_2}$ 3025, 1735, 1712, 1685 cm^{-1}; nmr δ 0.92, 1.20, 2.00 (singlets, 3 H each), 4.72 (broad multiplet, 1 H), 5.73 (singlet, 1 H).

Anal. Calcd for $C_{29}H_{40}O_4$: C, 76.95; H, 8.91. Found: C, 77.09; H, 8.95.

3β-Hydroxy-1′,2′-tetramethylene-16β,17α-[16,17-butanoandrosta-2′,5-dien]-4′-one (XXXIV).—To a solution of 1 g of 3β-hydroxypregn-5,16-dien-20-one in 25 ml of dry *t*-butyl alcohol containing 0.896 g of potassium *t*-butoxide was added 2 ml of cyclohexanone. After 15 min crystals began to form. After standing for 1.5 hr, the mixture was poured into a large volume of water with stirring. The resulting precipitate was removed by filtration and dried *in vacuo* giving 1.14 g of powder. This material was percolated through 5 g of Florisil. A fraction eluted with 5% ethyl acetate in chloroform crystallized from methanol to give 0.71 g of tiny plates, mp 230–232°. A pure sample prepared by vacuum sublimation at 210–215° (0.02 mm) had mp 238–240°; $[\alpha]D$ −7°; λ_{max} 239 mμ (14,000); $\nu_{max}^{CH_2Cl_2}$ 3600, 1670, 1605, 1040, 835 cm^{-1}; nmr δ 0.88, 1.05 (singlets, 3 H each), 3.49 (broad multiplet, 1 H), 5.35 (multiplet, 1 H), 5.70 (singlet, 1 H); *m/e* 394.2859 (calcd 394.2872).

Anal. Calcd for $C_{27}H_{38}O_2$: C, 82.18; H, 9.71. Found: C, 81.65; H, 9.74.

1′,2′-Tetramethylene-16β,17α-[16,17-butanoandrosta-2′,4-diene]-3,4′-dione (XXXV).—To a solution of 8 g of XXXIV in 500 ml of acetone at 10° was added with stirring 7.85 ml of a standard chromium trioxide reagent.[22] Nitrogen was bubbled through all solutions before and during the reaction. After 5 min the reaction mixture was diluted with 2500 ml of water and the resulting precipitate was filtered and dried to give 7.6 g of a white powder. The crude product was dissolved in 600 ml of warm methanol and 10 drops of 10% potassium hydroxide solution was added. This solution was heated on a steam bath for 10 min and neutralized with acetic acid. Concentration of this solution gave 6.5 g of crystals: mp 249–253°; $[\alpha]D$ +82°; λ_{max} 240 mμ (ε 28,900); $\nu_{max}^{CS_2}$ 3025, 1675, 1195, 860, 832 cm^{-1}; nmr δ 0.92, 1.22 (singlets, 3 H each), 5.74 (singlet, 2 H).

Anal. Calcd for $C_{27}H_{36}O_2$: C, 82.60; H, 9.24. Found: C, 82.36; H, 9.17.

3β-Acetoxy-1′,2′-trimethylene-5α,16β,17α-[16,17-butanoandrost-2′-ene]-4′,12-dione (XXXVI).—A mixture of 20 g of XXXI and 5.8 g of sodium methoxide in 200 ml of benzene was refluxed with stirring for 2 hr. The water formed was continuously removed using a Dean–Stark water trap. The mixture was cooled and the insoluble material was removed by filtration. The infrared spectrum of this material shows only saturated ketone absorption. The filtrate was evaporated to give 6.5 g of a syrupy residue. This material was refluxed in 30 ml of acetic anhydride for 2 hr and the liquid was removed *in vacuo*. The residue crystallized from methanol to give 5.4 g of crystals, mp 244–248°. A pure sample was prepared by vacuum sublimation at 215–220° (0.02 mm): mp 249–251°; $[\alpha]D$ +128°; λ_{max} 240 mμ (ε 13,800); $\nu_{max}^{CS_2}$ 3035, 1737, 1715, 1674, 1240, 1030 cm^{-1}; nmr δ 0.97, 1.19, 2.02 (singlets, 3 H each), 4.68 (broad multiplet, 1 H), 5.86 (singlet, 1 H); *m/e* 438.2767 (calcd 438.2769).

Anal. Calcd for $C_{28}H_{38}O_4$: C, 76.67; H, 8.73. Found: C, 76.25, H, 8.66.

Registry No.—I, 979-02-2; III, 2611-38-3; VII, 19459-49-5; VIII, 19459-50-8; IX, 6384-56-1; X, 18267-02-2; XI, 2724-68-7; XII, 19459-54-2; XIII, 1169-20-6; XIV, 19459-56-4; XX, 1434-54-4; XXI, 19459-58-6; XXII, 19459-59-7; XXIII, 19459-60-0; XXIV, 19459-61-1; XXV, 19459-62-2; XXVI, 19459-63-3; XXVII, 19459-64-4; XXVIII, 6953-90-8; XXIX, 19459-66-6; XXX, 19459-67-7; XXXI, 19459-68-8; XXXII, 19459-69-6; XXXIII, 19459-70-2; XXXIV, 19459-19-9; XXXV, 19459-20-2; XXXVI, 19459-21-3.

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16-Oxa Steroid. Synthesis and Structural Assignment

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Received October 3, 1968

A relatively simple procedure for the opening of ring D followed by the removal of C-16 was utilized for the synthesis of 16-oxa steroids.

The study of the effects of structural modifications of natural steriod hormones upon the biological activities has received considerable attention in the last few years and has led to a number of highly active synthetic modifications. Two recent publications[1,2] on the synthesis of 16-oxa steroid prompts us to report our work on the preparation of some of these compounds. In contrast to previous methods our procedure is stereospecific, consists of fewer steps and gives a higher yield. Moreover, one of the key intermediates (**3b**) in our synthetic project could be utilized in the synthesis of variety of heterocyclic steroids including D-nor oxa[3] and D-nor aza steroids.

The starting material in our synthesis is 3β-hydroxy-16,17-seco-16-norandrostan-15-(2′-indoxyliden)-17-oic acid (**2a**) which was obtained in 80% yield by allowing 3β-acetoxy-5α-androstan-17-one (**1**) to react with *o*-nitrobenzaldehyde, following essentially Hassner's procedure[4] (Scheme I).

Oxidation of methyl 3β-acetoxy-16,17-seco-16-norandrostan-15-(2′-indoxyliden)-17-oate (**2b**) with chromium trioxide in acetic acid at room temperature for 16 hr yielded 3β-hydroxy-15,17-seco-D-norandrostane-15,17-dioic acid 17-methyl ester (**3a**) in 75% yield. The compound on acetylation with acetic anhydride and pyridine gave the corresponding acetate **3b**. 3β-Acetoxy-15,17-seco-D-norandrostane-15,17-dioic acid 17-methyl ester, on treatment with diazomethane, gave the corresponding methyl ester **4**. The α configuration and the axial conformation of the 14 hydrogen in compounds **3a**, **3b**, and **4** is based on the observation of a doublet center around δ 2.5 in the nmr spectrum having a *coupling constant of 10.5 cps* which is characteristic of *trans-diaxial hydrogens*.

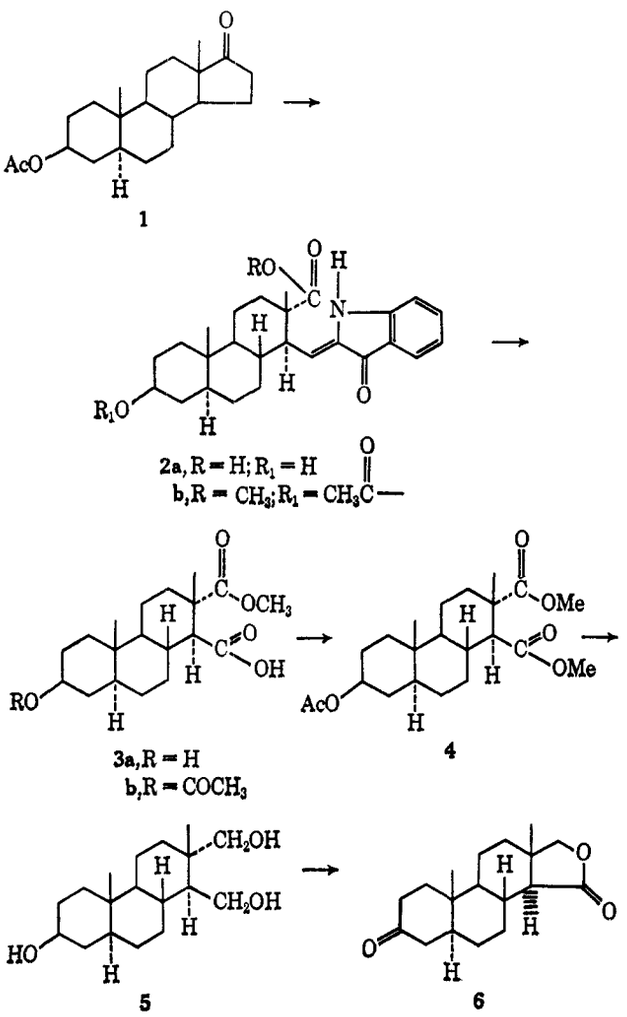
(1) R. W. Kierstead and A. Faraone, *J. Org. Chem.*, **32**, 705 (1967).
(2) J. S. Baran, *J. Med. Chem.*, **10**, 1039 (1967).
(3) A. K. Banerjee and M. Gut, *Tetrahedron Lett.* 51, (1969).
(4) A. Hassner, M. J. Haddadin, and P. Catsoulacos, *J. Org. Chem.*, **31**, 1363 (1966).

Table I

Compound	Predicted from sector rule	Exptl sign	Amplitude
16-Oxo-5α-androstane-3,15-dione	+	+	ϕ_{225} +3,183
16-Oxa-5α-androstane-3,17-dione[a]	+	+	ϕ_{223} +2,970
3β-Hydroxy-5α,14β-isoandrostan-15-one	−	−	ϕ_{220} −19,800
3β,15β-Dihydroxy-16-oxa-5α,14β-isoandrostan-17-one 3-acetate[b]	−	−	ϕ_{226} −5,320
3β-Acetoxy-17-oxa-5α-androstan-16-one[c]	−	−	ϕ_{221} −5,362

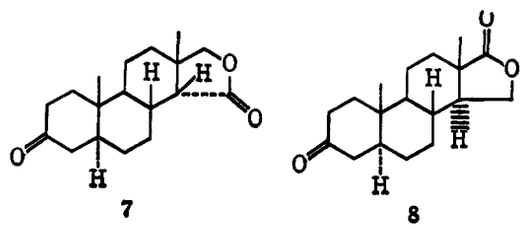
[a] Kindly supplied by Dr. R. W. Kierstead, Hoffmann-La-Roche Inc., Nutley, N.J., [b] Unpublished work by A. K. Banerjee. [c] S. Rakhit and M. Gut, *J. Org. Chem.*, **29**, 229 (1964).

Scheme I

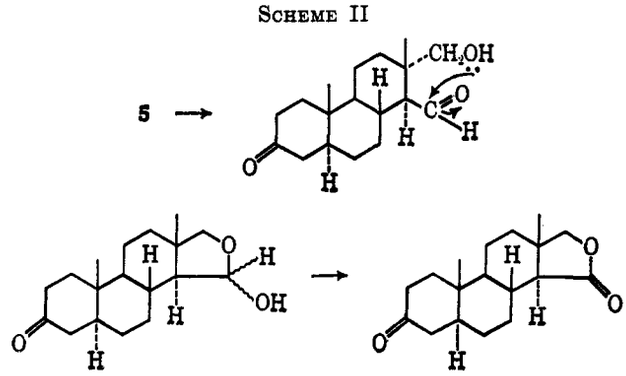


3β-Hydroxy-15,17-seco-D-norandrostane-15,17-dioic acid dimethyl ester, on reduction with lithium hydride in tetrahydrofuran, gave 15,17-seco-D-norandrostane-3β,15,17-triol (**5**), which on oxidation with Jones reagent[5] gave almost quantitatively lactone **6**: ν_{max}^{KBr} 5.70 (γ-lactone) and 5.90 (3-ketone). Its nmr spectrum in deuteriochloroform showed an ill-defined quartet for a 2-hydrogen center around δ 3.91 which could be assigned to the 17 hydrogens. The quartet became clear and distinct when the solvent was changed from deuteriochloroform to benzene. It is conceivable that compound **5** on oxidation could give rise to either of the products **6**, **7** or **8**.

The nmr spectrum of **8** would show the presence of ABX system whereas **6** and **7** would show the AB system. Since the lactone showed a quartet, its structure could be either **6** or **7**. From the discussion (see below) of the ORD (lactone region) which showed a positive Cotton effect, it can be stated that the lactone is best represented by **6**. The exclusive formation of **6** rather than **8** can be explained from steric considerations and could be mechanistically expressed as in Scheme II.



Scheme II



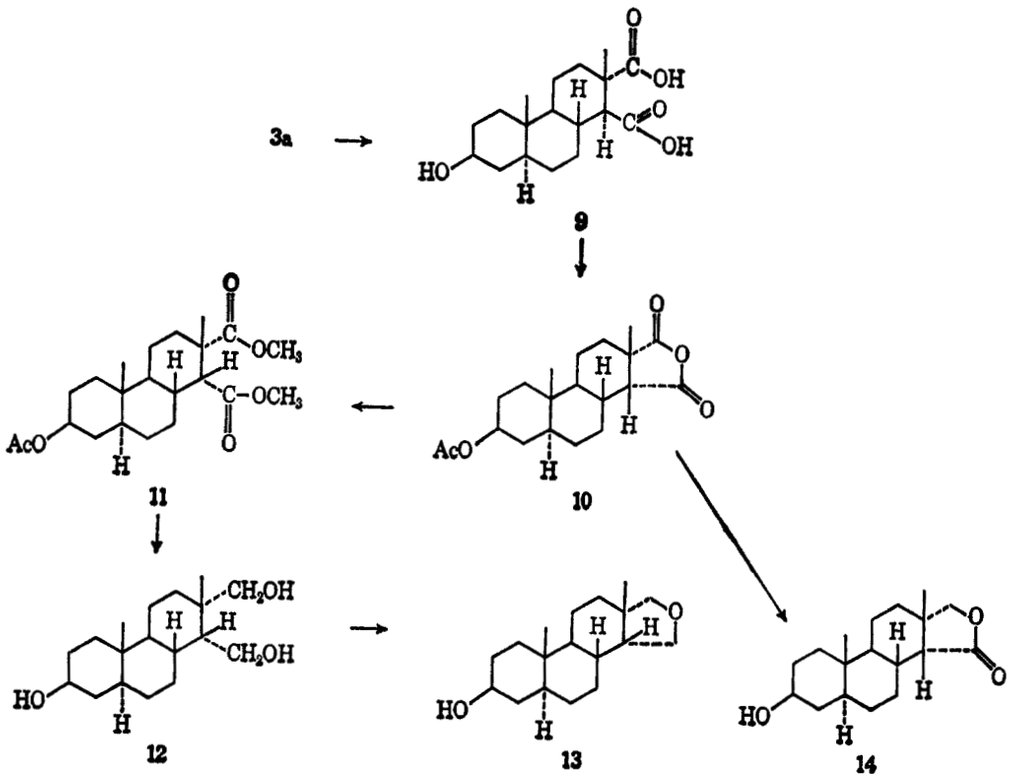
At this stage it was desirable to prepare stereospecifically the two 14 isomers and compare their spectral properties (Scheme III).

3β-Hydroxy-15,17-seco-D-norandrostane-15,17-dioic acid 17-methyl ester **3a**, upon refluxing with 20% methanolic potassium hydroxide for 48 hr, gave dibasic acid **9**, which, on treatment with boiling acetic anhydride, gave a cyclic anhydride: ν_{max}^{KBr} 5.40, 5.61, 5.80 and 8.00 μ. The *cis* configuration of anhydride **10** is based on the following observations. (a) The nmr spectrum showed the presence of a doublet center around δ 2.69, having a coupling constant, J = 2.5 cps, which confirmed the presence of a 14β hydrogen (axial–equitorial coupling). (b) The anhydride, on treatment with anhydrous methanol, gave a mixture of half-esters which, on methylation with diazomethane, gave a single diester **11**. It has a infrared spectrum similar to that of **4**, but differs considerably in its nmr spectrum, *i.e.*, the presence of a doublet center around δ 2.69 having J = 2.5 cps in contrast to the doublet at δ 2.50 having J = 10.5 cps in the *trans* series. Its fragmentation pattern in the mass spectrum corresponds to that of the *trans* series.

The exclusive formation of one anhydride under the

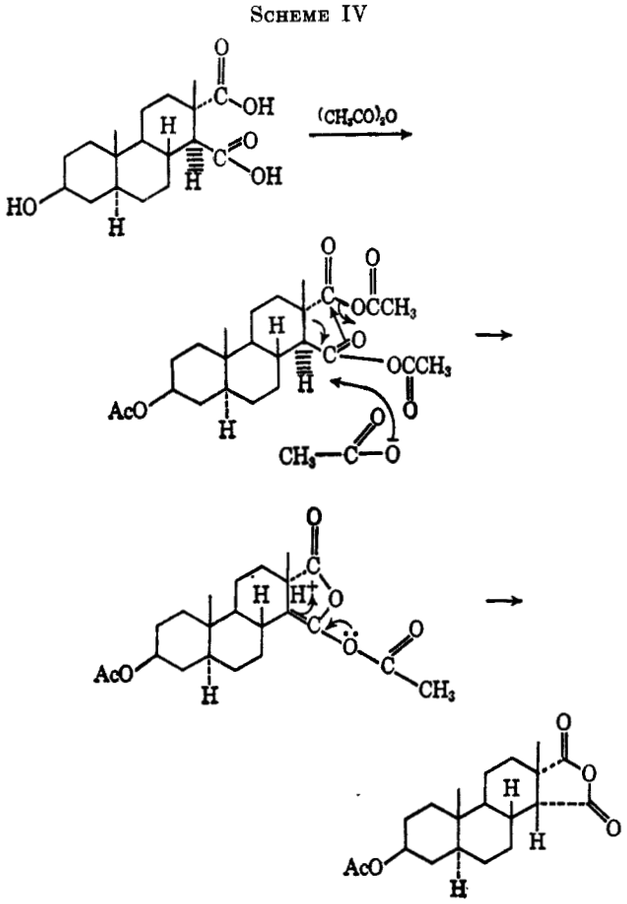
(5) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. Weeden, *J. Chem. Soc.*, **39**, (1946).

SCHEME III



reaction conditions is rather interesting. Examination of Dreiding models shows that both the *cis* and *trans* anhydride are free of strain. Since our starting material was the *trans* dibasic acid, the exclusive formation of the *cis* anhydride may be illustrated by Scheme IV.

SCHEME IV



Diester **11**, on reduction with lithium aluminum hydride in refluxing tetrahydrofuran for 16 hr, gave 15,17-seco-14-iso-D-norandrostane-3β,15,17-triol (**12**) (80% yield), which upon treatment with dimethyl sulfoxide[6] at 150° for 6 hr gave 16-oxa compound **13**. Lithium aluminum hydride reduction of anhydride **10** gave[7] besides other products a lactone to which structure **14** was assigned on the basis of the following observations: ν_{max}^{KBr} 2.85 (-OH) and 5.70 (γ-lactone); nmr δ 3.68 (2 H, singlet 17-H's) and 2.10 (1 H, doublet $J_{axial-equitorial}$ = 2.5 cps, 14β-H).

In recent years Klyne[8] and his coworkers have utilized the ORD method for the determination of the configuration of lactones. By applying the lactone sector rule it became possible to predict correctly the sign of the Cotton effect. Application of the lactone sector rule to the following lactones showed that the predicted values agreed well with the experimental data (Table I).

Experimental Section

Unless otherwise stated, combustion analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y. Melting points were taken on a Fisher-Johns hot stage and were not corrected. The infrared spectra were recorded from a pressed potassium bromide pellet on a Perkin-Elmer Infracord spectrophotometer; nmr spectra were obtained on a Varian V-4300 B spectrophotometer in deuteriochloroform solution using tetramethylsilane as internal standard. Mass spectra were recorded on a Varian M-66 mass spectrometer. Preparative layer chromatography was done on a 20 × 20 cm and 20 × 40 cm plate with a thickness of 2.5 mm using silica gel H_{254} (Brinkmann).

3β-Hydroxy-16,17-seco-16-norandrostan-15-(2'-indoxyliden)-

(6) B. T. Grillis and P. E. Beck, *J. Org. Chem.*, **28**, 1388 (1963).

(7) For discussion of mechanism, see J. J. Bloomfield and S. L. Lee, *ibid.*, **32**, 3919 (1967).

(8) W. Klyne and P. M. Scopes in "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," G. Snatzke, Ed., Heyden & Son Ltd., London, 1967, Chapter 12, p 193.

17-oic Acid (2a).—To a solution of 5 g of 3β-acetoxyandrostan-17-one (1) in 150 ml of 3% methanolic potassium hydroxide, there was added a solution of 3 g of *o*-nitrobenzaldehyde in 10 ml of methanol. The solution was stirred at room temperature under nitrogen for 18 hr, then diluted with water and acidified with 2 *N* hydrochloric acid. The resulting yellow precipitate was collected by filtration, washed repeatedly with water and dried. Recrystallization from methanol–water gave 4.5 g of bright yellow crystals, mp 260–262° dec (lit.[4] mp 258–260° dec). A second crop of 500 mg was obtained, mp 260–262° dec (total yield 79%). In several runs the yield varied from 75 to 85%.

3β-Hydroxy-16,17-seco-16-norandrostan-15-(2′-indoxyliden)-17-oic Acid 17-Methyl Ester (2b) and Its 3β-Acetate (2c).—Methyl ester **2b** was obtained in almost quantitative yield from acid **2a** with diazomethane by the usual procedure. Crystallization from methylene chloride–ether afforded bright yellow prisms, mp 262–264° (lit.i mp 263–265°).

Acetylation with acetic anhydride–pyridine gave yellow needles, **2c**, mp 262–264° (lit.[4] mp 261–262°), in almost quantitative yield.

3β-Hydroxy-15,17-seco-D-norandrostane-15,17-dioic Acid 17-Methyl Ester (3a).—To a solution of 6 g of **2b** in 250 ml of glacial acetic acid there was added slowly a solution of 4.5 g of chromium trioxide in 5 ml of water under nitrogen. The yellow solution turned reddish brown with evolution of heat (the temperature was kept below 60° by external cooling). After stirring overnight at room temperature under nitrogen, the solution was diluted with 750 ml of water and the resulting turbid solution was thoroughly extracted three times with 150 ml of ether. The yellow ether layer was repeatedly washed with water to remove the isatin. The ethereal layer was then extracted three times with 50 ml of 2 *N* sodium hydroxide solution. Acidification of the basic solution with 2 *N* hydrochloric acid precipitated **3a** as a white solid. This was filtered, washed thoroughly with water and dried. One crystallization from aqueous methanol (Norit) gave 3.2 g (66%) of needles, mp 232–234°. In several runs the yield varied from 65 to 70%. An analytical sample was prepared by crystallizing from methanol–water to give needles: mp 234–235°; ν_{max} 2.82 (–OH), 3.00–3.10 (hydrogen bonded $-CO_2H$), 5.78 (methyl ester) and 5.85 and 5.90 μ (broad, unbonded and bonded CO_2H); nmr (pyridine) δ 3.64 (3 H, singlet, 17-CO_2Me), 2.86 (1 H, doublet, J = 10.5 cps, 14α-H), 1.00 (3 H, singlet, 18-methyl) and 0.82 (3 H, singlet, 19-methyl); mass spectrum (70 eV) *m/e* 338 (M^+), 320 $(M - H_2O)^+$ and 306 $(M - MeOH)^+$.

Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.94. Found: C, 67.37, H, 8.81.

3β-Acetoxy-15,17-seco-D-norandrostane-15,17-dioic Acid 17-Methyl Ester (3b).—The solution of 10 g of **3a** in 15 ml of anhydrous pyridine was added to 15 ml of acetic anhydride, the flask stoppered and left overnight at room temperature. It was then poured onto crushed ice containing 20 ml of methanol and 15 ml of 2 *N* hydrochloric acid. After standing at room temperature for 1 hr, the acetate slowly crystallized out. It was filtered, washed repeatedly with water and dried. On crystallization from acetone–benzene it gave 10 g (95%) of prisms, mp 203–204°. An analytical sample was crystallized from ether–hexane: mp 205–207°; ν_{max} 3.15 (hydrogen-bonded CO_2H), 5.78 (acetate and methyl ester) and 5.9 μ (CO_2H); nmr δ 4.65 (1 H, multiplet, 3α-H), 3.63 (3 H, singlet, 17-CO_2Me), 2.56 (1 H, doublets, J = 10.5 cps, 14α-H), 2.01 (3 H, singlet, 3β-$OCOCH_3$), 1.26 (3 H, singlet, 18-methyl) and 0.82 (3 H, singlet, 19-methyl); mass spectrum (70 eV) *m/e* no molecular ion peak 348 $(M - MeOH)^+$ 320 $(M -$ acetic acid$)^+$.

Anal. Calcd for $C_{21}H_{32}O_6$: C, 66.30; H, 8.48. Found: C, 66.57; H, 8.50.

3β-Acetoxy-15,17-seco-D-norandrostane-15,17-dioic Acid Dimethyl Ester (4).—Methylation of 1 g of **3b** with diazomethane by the usual procedure gave, upon removal of the solvent, an oil which was obtained in almost quantitative yield. It crystallized from aqueous methanol in needles, mp 118–120°. An analytical sample was crystallized from methanol–water: mp 120–121°; ν_{max} 5.79 μ (broad, acetate and methyl ester); nmr δ 4.65 (1 H, multiplet, 3α-H), 3.62 (3 H, singlet, 15-CO_2CH_3), 3.59 (3 H, singlet, 17-CO_2Me), 2.50 (1 H, doublet, J = 10 cps, 14α-H), 2.00 (3 H, singlet, 3β-$OCOCH_3$), 1.20 (3 H, singlet, 18-methyl), and 0.82 (3 H, singlet, 19-methyl); mass spectrum (70 eV) *m/e* 394 (M^+), 362 $(M - CH_3OH)^+$ base peak.

Anal. Calcd for $C_{22}H_{34}O_6$: C, 66.98; H, 8.69. Found: C, 67.04; H, 8.72.

15,17-Seco-D-norandrostane-3β,15,17-triol (5).—A solution of 500 mg of **3b**, in 5 ml of anhydrous tetrahydrofuran was added to the suspension of 500 mg of lithium aluminum hydride in 30 ml of anhydrous tetrahydrofuran in a three-necked flask, fitted with a reflux condenser, dropping funnel and nitrogen inlet dropwise, during 20 min. The mixture was then refluxed for 16 hr and then the excess of lithium aluminum hydride was decomposed by following the procedure of Micovic and Mihailovic.[9] The mixture was filtered, the residue washed with a small amount of tetrahydrofuran and then the filtrate was evaporated under vacuum whereby a crystalline solid was obtained. The residue was suspended in water, filtered, washed with water and dried to give 300 mg (80%) of crude **5**. On crystallization from acetone it gave rectangular plates: mp 228–230°; ν_{max} 2.85 μ (OH); nmr [$CD_3S(\rightarrow O)CD_3$] δ 3.50 (4 H, broad, 15- and 17-CH_2OH) and 0.75 (6 H, two superimposed singlets, 18 and 19 methyl; mass spectrum (70 eV) *m/e* 278 $(M - H_2O)^+$ and 265 $(M - CH_2OH)^+$.

Anal. Calcd for $C_{18}H_{32}O_3$: C, 72.92; H, 10.88. Found: C, 72.98; H, 10.98.

16-Oxa-5α-androstane-3,15-dione (6).—The solution of 200 mg of **5** in 20 ml of anhydrous acetone was cooled to 0° and to this Jones reagent[5] was added dropwise (until the faint color of the reagent persists) over a period of 5 min. It was then allowed to stand an additional 10 min at 0°. The mixture was then poured into ice water and extracted with ether. The etheral layer was washed sodium bicarbonate, water and dried. On removal of the solvent 180 mg (91%) of oil was obtained which could be crystallized. On recrystallization from methanol it gave needles: mp 165–166°; ν_{max} 5.70 (γ-lactone) and 5.90 μ (3-ketone); nmr δ 3.90 (2 H, quartet, 17-H's and 1.08 (6 H, two superimposed singlet, 18- and 19-methyl); mass spectrum (70 eV) *m/e* 290 M^+.

Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.48; H, 8.90. Found: C, 74.40; H, 8.86.

3β-Hydroxy-15,17-seco-D-norandrostane-15,17-dioic Acid (9).—To the solution of 2 g of **3a** in 5 ml of methanol was added 40 ml of 20% methanolic potassium hydroxide and refluxed for 48 hr under nitrogen. It was then cooled, diluted with 50 ml of water and acidified, whereby a white precipitate was obtained. This was filtered, washed repeatedly with water and dried to give 1.6 g (84%) of **9**. Crystallization from methanol–water furnished white flakes: mp 225–256° (one more recrystallization raised the melting point to 256–258°); ν_{max} 2.85 (OH), 3.00–3.15 (broad CO_2H) and 5.9 μ (broad CO_2H); nmr [$CD_3S(\rightarrow O)CD_3$], 3.65 (1 H, multiplet, 3α-H), 2.35 (1 H, doublet, J = 10.8, 14α-H), 1.10 (3 H, singlet, 18-methyl) and 0.75 (3 H, singlet, 19-methyl); mass spectrum (70 eV), no molecular ion peak, *m/e* 306 $(M - H_2O)^+$, 288 $(M - 2H_2O)$.

Anal. Calcd for $C_{18}H_{28}O_5 \cdot MeOH$: C, 66.64; H, 8.70. Found: C, 66.46, H, 8.60.

3β-Acetoxy-15,17-diketo-16-nor-16-oxa-14β-androstane (10).—The solution of 1 g of **9** in 10 ml of acetic anhydride was refluxed for 6 hr. Excess acetic anhydride and the small amount of acetic acid formed during the reaction were removed under vacuum when 600 mg (59%) of crystalline solid was obtained. This was crystallized from ether–hexane in rectangular plates, mp 208–210°. An analytical sample, mp 210–212°, was obtained by further recrystallizations: ν_{max} 3.43, 5.40, 5.61, 5.80 and 8.00 μ; nmr δ 4.65 (1 H, multiplet, 3α-H), 2.77 (1 H, doublet, J = 2.5 cps, 14β-H), 2.01 (3 H, singlet, 3β-$OCOCH_3$), 1.38 (3 H, singlet, 18-methyl) and 0.81 (3 H, singlet, 19-methyl); mass spectrum (70 eV), no molecular ion peak, *m/e* 288 base peak $(M -$ acetic acid$)^+$, 273 $(M -$ methylacetic acid$)^+$.

Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.87; H, 7.95.

3β-Acetoxy-15,17-seco-D-nor-14-isoandrostane-15,17-dioic Acid Dimethyl Ester (11).—The solution of 500 mg of **10** in 20 ml of anhydrous methanol refluxed for 4 hr (reflux was continued until disappearance of the anhydride band in the infrared spectrum) and then the solvent was removed under vacuum, whereby a crystalline solid was obtained. A thin layer chromatography, using the solvents methylene chloride–methanol–acetic acid (95:4:1) gave a plate that showed two spots, indicating that the mixture contained the two half-esters. No attempt was made to separate them. The eluate gave a crude solid of 500 mg

(9) V. M. Micovic and M. L. Mihailovic, *J. Org. Chem.*, **18**, 1190 (1953).

which was dissolved in ether and methylated with diazomethane in the usual way. The crude diester was crystallized from methanol–water, giving pure **11**, mp 120–21°. An analytical sample was prepared by recrystallization from aqueous methanol: mp 121–122°; ν_{max} 5.80 (acetate and methyl ester) and 8.00 μ; nmr δ 3.63 (1 H, multiplet, 3α-H), 3.60 (6 H, singlet, 15-COOCH$_3$ and 17-COOCH$_3$), 2.00 (3 H, singlet, 3β-OCOCH$_3$), 2.69 (1 H, doublet, J = 2.5 cps, 14β-H), 1.26 (3 H, singlet, 18-methyl) and 0.81 (3 H, singlet, 19-methyl); mass spectrum (70 eV) m/e 394 (M^+, strong), 362 [$(M - CH_3OH)^+$, weak].

Anal. Calcd for $C_{22}H_{34}O_6$: C, 66.98; H, 8.69. Found: C, 66.78; H, 8.59.

15,17-Seco-D-nor-14-isoandrostane-3β,15,17-triol (12).—To the suspension of 500 mg of lithium aluminum hydride in 30 ml of anhydrous tetrahydrofuran was added 500 mg of **11**, dissolved in 5 ml of anhydrous tetrahydrofuran, over a period of 15 min. The mixture was then heated under reflux under nitrogen for 16 hr. Excess of reagent was decomposed following the procedure of Micovic and Mihailovic.[9] It was then filtered, washed with a small amount of tetrahydrofuran and the filtrate along with the washings were concentrated under vacuum, when a crystalline solid was obtained. The mixture was diluted with water, filtered and the residue was washed thoroughly with water and dried to give 300 mg (80%) of **12**. Recrystallization from methanol gave needles: mp 263–264° (transformation at 250°); ν_{max} 2.98, 3.42, 9.55, 9.71 and 10.9 μ; nmr[$CD_3(S\rightarrow O)CD_3$] δ 0.93 (3 H, singlet, 18-methyl) and 0.70 (3 H, singlet, 19-methyl), mass spectrum (70 eV) m/e 278 $(M - 18)^+$.

Anal. Calcd for $C_{19}H_{32}O_3$: C, 72.98; H, 10.88. Found: C, 72.78, H, 10.68.

3β-Hydroxy-16-oxa-16-nor-5α-androstane (13).—The solution of 150 mg of **12** in 5 ml of anhydrous dimethyl sulfoxide was heated at 150° for 6 hr. It was then cooled, diluted with 15 ml of water and extracted with ether. The etheral extract was washed thoroughly with water and dried over sodium sulfate. On removal of solvent, an oil was obtained, which was purified through preparative thick layer chromatography using the system ethyl acetate–benzene 15:85. After elution a crystalline solid was obtained, which was recrystallized from aqueous methanol to give needles: mp 163–164°; ν_{max} 2.85 (OH) and 9.00 μ; mass spectrum (70 eV) m/e 278 (M^+), 260 $(M - 18)^+$.

Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.36; H, 10.68.

3β-Hydroxy-16-oxa-5α,14β-androstan-15-one (14).—To the suspension of 300 mg of lithium aluminum hydride in 30 ml of anhydrous tetrahydrofuran was added over a period of 15 min 300 mg of **8**, dissolved in 5 ml of anhydrous tetrahydrofuran. The mixture was refluxed overnight under nitrogen. It was then cooled and the excess of reagent was decomposed by following the procedure of Micovic and Mihailovic.[9] The mixture was then filtered, washed with a small amount of tetrahydrofuran and the filtrate along with its washings was concentrated under vacuum when a crystalline solid was obtained. More solids were precipitated when 10 ml of water was added to the filtrate. The solids were collected by filtration, washed repeatedly with water and dried. Recrystallization from methylene chloride–hexane gave needles: mp 208–210°; ν_{max} 2.85 (OH) and 5.40 μ (γ-lactone); nmr δ 3.78 (2 H, singlet, 17-H's), 2.10 (1 H, doublet, J = 3 cps, 14β-H), 1.29 (3 H, singlet 18-methyl), and 0.80 (3 H, singlet, 19-methyl); mass spectrum (70 eV) m/e at 292 (M^+).

Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.69; H, 9.55.

Registry No.—**3a**, 19018-69-0; **3b**, 19018-70-3; **4**, 19018-71-4; **5**, 19018-72-5; **6**, 19018-73-6; **9**, 19018-74-7; **10**, 19018-75-8; **11**, 19018-76-9; **12**, 19018-77-0; **13**, 19018-78-1; **14**, 19018-79-2.

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Lead Tetraacetate Oxidation of the Oxime of Pregna-5,16-dien-3β-acetoxy-20-one[1]

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Since the lead tetraacetate promoted free-radical reaction between a secondary hydroxyl group and an otherwise nonactivated hydrogen atom was first described in the steroid series by Jeger, *et al.*,[3] many similar reactions have been reported in the literature.[4]

A modification of the method was introduced by Heusler, *et al.*,[5] who added iodine to the reaction medium. Under these conditions both alternate products and a different reaction mechanism are often observed. It was of interest to determine if similar transformations could be achieved with a hydroxyl group attached to nitrogen. As an example we selected the oxime of 3β-acetoxypregna-5,16-dien-20-one (I) (Scheme I) which could possibly lead to heterocyclic products of biological interest. Treatment of oxime I with lead tetraacetate in dry benzene and also in the presence of iodine gave a high-melting crystalline compound as the major product. A dimeric structure II was assigned to this compound on the basis of the following spectroscopic evidence (Scheme I).

In the mass spectrum of II, there are peaks at m/e 680 and 620 clearly indicating the dimeric nature of the sample with a one degree higher oxidation state than the corresponding monomer (ion m/e 680 = 2 × monomer

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