column A, 1689; I_K^P, column C, 2196; infrared spectrum (Figure 1); 5.6% of oil (8.7 ppm in plant), peak areas from SE-30 glpc.[1] *Anal.* Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.83; H, 11.70.

Pmr analyses showed 0.85 d (3, 6.5), 1.36 (1), 1.57 (3), 1.63 (6), 1.92 m, br (6), 2.24 m, br (1), 5.08 t, br (1, 6.5), 5.20 m, br (1); mass spectrum *m/e* (intensity), 222 (2, parent), 204 (23), 122 (21), 121 (39), 119 (40), 111 (38), 93 (61), 82 (33), 81 (100), 72 (31), 69 (44), 67 (26), 55 (31), 41 (55), 32 (40), 28 (36).

The pmr spectrum of the (trichloroacetyl) carbamate of **1**, obtained within 10 min after addition of 4 drops of trichloroacetyl isocyanate to **1** in CCl_4 in the pmr tube,[11] showed the following:[13] 0.94, d (3, 6.5); 1.58 d (3, ~1); 1.67 (6); 1.75 d, br (2, 7); 1.99 m, br (4); 2.37 br, m (4); 2.65 br (1) 5.02 br, t (1, 7.5); 5.23 br (1); 8.43 br (1).

The [*p*-(phenylazo)phenyl]urethan (mp 96–99°, from pentane) formed readily.[15] *Anal.* Calcd for $C_{25}H_{35}N_3O_2$: C, 75.47; H, 7.92; N, 9.43. Found: C, 75.61; H, 7.94; N, 9.61.

Dehydration of 1.—Phthalic anhydride (1.5 g, 10 mmoles) and crude **1** (1.11 g, 5.0 mmoles) were heated at 120–175° for 1 hr under reduced pressure in a Bantamware still without any apparent distillation of hydrocarbon. The reaction mixture was extracted with pentane, filtered, and the solvent removed under reduced pressure. Glpc (column B)[13] of the residue taken up in pentane showed several major peaks. The entire pentane solution (*ca.* 1 ml) was chromatographed (B) in four injections and four fractions were trapped into CCl_4 (Table II). Only fractions D2 and D3 contained enough sample to give useful pmr spectra. The D2 spectrum contained signals interpreted as belonging to **8**; D3 appeared to be principally **7**. Rechromatography and trapping of D2 and D3 into CCl_4 was conducted on column A. I_K^P and I_K^A values of each fraction and subfraction are given in Table II. The signals attributed to **8** in D2 were nearly absent in D2-2, but too little D2-1 (presumed to be **8**) was trapped to obtain a pmr spectrum. D3, initially lacking any aromatic components, gave rise to **7** (D3-2), **9** (D3-1), and an originally present but unidentified component, D3-3. Pmr analyses of **7** showed the following: 0.94 d (3, 6.5); 1.52 (3); 1.60 (8); 1.95 m, br (2); 2.24 m, br (1); 2.49 (4); 5.01 m, br (1); 5.32 br (2). Pmr analyses of **8** showed the following: 0.96 d (3, 6.5); 1.71 (3); 1.99 (4); 5.48 br (2). Pmr analyses of **9** showed the following: 1.16 d (3, 6.5); 1.46 (3); 1.61 br (5); 1.91 br (2); 2.25 (3); 2.79 m, br (1); 5.0 br (1); 6.93 (4).

TABLE II

GLPC FRACTIONS OBTAINED FROM DEHYDRATION OF β-BISABOLOL

Peak (column)[a]	I_K^P, 175°	I_K^A, 175°	Fraction designation	Dehydr prods,[b] %
1(B)	1646	...	D1	6
2(B)	1655	...	D1	5
3(B), 1(A)	1728	1496	D2-1	3
3(B), 2(A)	1728	1513	D2-2	33
4(B), 1(A)	1775	1489	D3-1	0,[c] 13[d]
4(B), 2(A)	1775	1515	D3-2	25,[c] 14[d]
4(B), 3(A)	1775	1531	D3-3	10,[c] 8[d]
5(B)	1811	...	D4	7

[a] See ref 13. [b] Triangulation of peak areas and normalization of total area to 100. [c] % present in D3 mixture before glpc on column A. [d] % present after rechromatography of D3 on column A.

Tetrahydro-β-bisabolol (2, 3).—Quantitative reduction of **1** (2.546 g, 11.5 mmoles) in pentane was accomplished at 3.5 atm of H_2 over Pd on charcoal. Three peaks (I_K^P1837, 1930, 1937) in ratio 1:85:14 appeared upon glpc (column C)[13] of the reduction mixture after solvent removal. Each of these was trapped separately into CCl_4 from 120 μl of the mixture. Tlc of these fractions (silica gel G–benzene) demonstrated that the 1930 peak was a mixture of two materials, **2** and **3**; ratio 3:1, R_f 0.25 and 0.41. Preparative tlc and glpc gave I_K^P (column C) 1932 and 1928; I_K^A (column A) 1621 and 1636, respectively. The infrared spectrum of this mixture matched that of 1-(1′,5′-dimethylhexyl)-4-methylcyclohexanol[10] with only several minor differences: mass spectrum (I_K^P 1930 mixture) m/e (intensity), 226 (1, parent), 208 (3), 124 (17), 123 (13), 113 (100), 95 (44), 81 (12), 69 (5), 67 (5), 55 (7), 41 (7). Pmr analyses (I_K^P 1930 mixture) showed the following: 0.71 (1); 0.82 d (3, 6.5); 0.85 d (9, 6.5); 1.05 (1); 1.21 br (6); 1.54 br, m (2); 1.72 br, m (3).

After the pmr spectrum of the mixture of **2** and **3** had been obtained, 4 drops of trichloroacetyl isocyanate were added to the sample in the pmr tube. The spectrum of the carbamate was run within 10 min of derivatization, which was complete at that time. Pmr analysis (I_K^P 1930 mixture plus isocyanate) showed the following: 0.89 d (3, 6.5); 0.96 d (9, 6.5); 1.27 br (6); 1.43 br (4); 1.75 br (2); 1.92 br (2); 2.21 m, br (3); 8.61 br (1).

Bisabolane (4, 5).—The crude reduction mixture (1.123 g, 4.23 mmoles of **2** plus **3**) and phthalic anhydride (1.5 g, 10 mmoles) were heated together at 135° for 30 min. The mixture was washed with 40 ml of 5% Na_2CO_3 solution and extracted with pentane (50 ml, three portions). After solvent removal under reduced pressure and drying (Na_2SO_4), 0.7 ml of a pale yellow oil was obtained. Tlc on silica gel with benzene revealed only small amounts of nonhydrocarbon impurities. Chromatography on an Alcoa F-20 alumina column (2.0 × 10 cm) with 200 ml of pentane, followed by pentane removal under reduced pressure, afforded 0.5 ml of a pale yellow oil. This was taken up in 15 ml of pentane and hydrogenated at 3.5 atm over palladium on charcoal. Filtration from the catalyst and pentane removal (reduced pressure) gave 0.4–0.5 ml of a crystal clear oil. Glpc (columns B and A) demonstrated that this oil was a mixture of two incompletely resolved components: ratio 4:1; I_K^P 1508, 1526; I_K^A 1475, **5** and **4**, respectively.

Glpc behavior and infrared and mass spectra of this hydrocarbon mixture were identical with those of authentic bisabolane from reduction of **6** from cotton oil.[4] Its infrared spectrum was also identical with a reported spectrum of bisabolane:[9] mass spectrum *m/e* (intensity), 210 (9, parent), 125 (22), 124 (16), 112 (13), 97 (100), 96 (83), 83 (15), 81 (34), 71 (12), 69 (46), 67 (10), 57 (34), 56 (22), 55 (82), 43 (17), 41 (27).

Registry No.—**1**, 15352-77-9; **1** (trichloroacetyl)carbamate, 15352-78-0; **2**, 15352-79-1; **2** (trichloroacetyl)-carbamate, 15352-80-4; **3**, 15352-81-5; **3** (trichloroacetyl)carbamate, 15352-82-6; **4**, 11042-77-6; **5**, 11042-76-5; **6**, 11037-64-2; 4-terpinenol, 562-74-3; **7**, 11037-65-3; γ-terpinene, 99-85-4; **8**, 11037-66-4; α-terpinene, 99-86-5; **9**, 11012-67-2; *p*-cymene, 99-87-6.

(15) J. A. Attaway, R. W. Wolford, G. E. Alberding, and G. J. Edwards, *Anal. Chem.*, **35**, 234 (1963).

Steroid Hormone Analogs. IV.[1] C-Nor-D-homoestrone[2]

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Interest continues in the synthesis of modified steroids in a search for analogs with enhanced or more specific pharmacological properties. During the past few years, several groups have reported studies of the synthesis of C-nor-D-homo steroid hormone analogs.[1,3–7] We describe herewith the synthesis of the

(1) Part III in the series: S. M. Kupchan and M. J. Abu El-haj, *J. Org. Chem.*, **33**, 647 (1968).

(2) This investigation was supported in part by Public Health Service Research Grant HE-02275 from the National Heart Institute.

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(6) W. F. Johns and I. Laos, *J. Org. Chem.*, **30**, 4220 (1965), and the references cited there.

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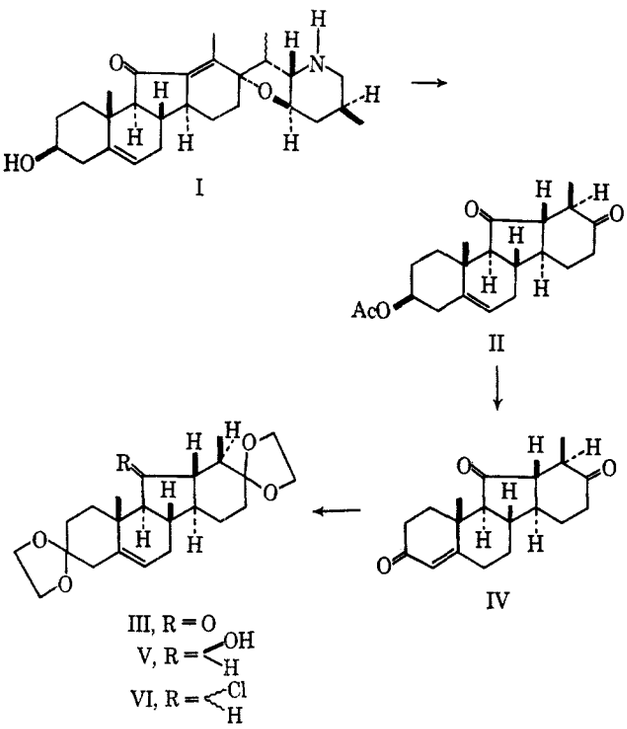
C-nor-D-homoestrone derivative XIV, which possesses the estrone configuration at each of the ring junctions.

The readily available veratrum alkaloid jervine (I)[8] was converted *via* Δ^5-etiojerven-3β-ol-11,17-dione 3-acetate (II) into Δ^4-etiojervene-3,11,17-trione (IV)[3] (Scheme I). In an approach aimed at a $\Delta^{9(11)}$-ene derivative (for ring A aromatization by the Tsuda method[9]), IV was converted into diketal III, which, in turn, was reduced with lithium aluminum hydride to V. However, attempts to dehydrate V with thionyl chloride or phosphorus oxychloride were unsuccessful and yielded instead a chloro derivative (VI).

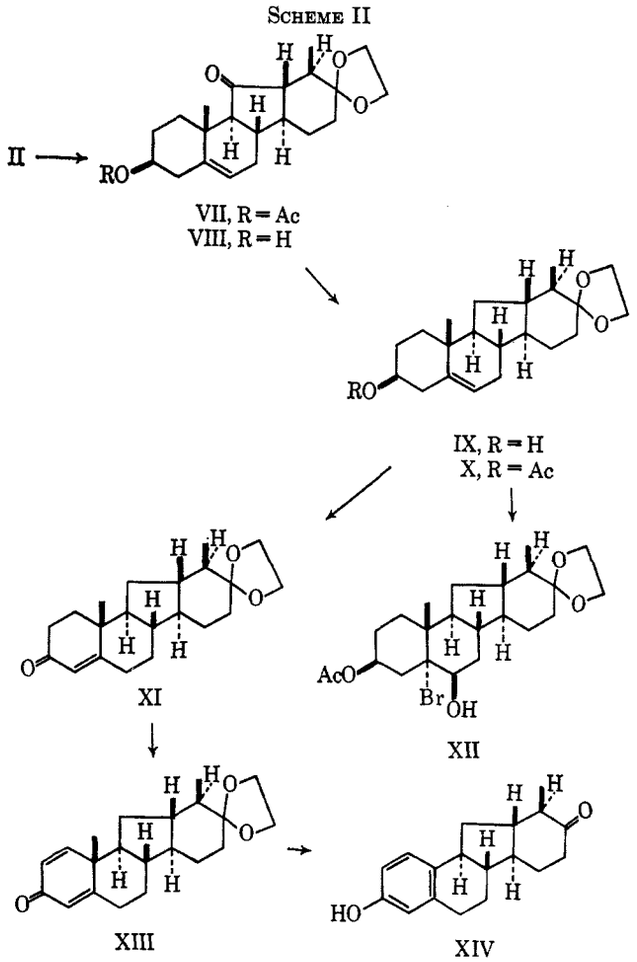
SCHEME I



The successful route to the C-nor-D-homoestrone (XIV) proceeded *via* ketalization of II to Δ^5-etiojerven-3β-ol-11,17-dione 17-monoethylene ketal 3-acetate (VII). A polar impurity VIII in the ketalization reaction was shown to be the saponification product of VII. When VII was subjected to Wolff–Kishner conditions, the compound was reduced to Δ^5-etiojerven-3β-ol-17-one 17-ethylene ketal (IX) and Oppenauer oxidation of IX gave the conjugated ketone XI (Scheme II). Subsequent treatment of XI with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dioxane produced $\Delta^{1,4}$-etiojervadiene-3,17-dione 17-monoethylene ketal (XIII). Finally, the desired C-nor-D-homoestrone (XIV) was obtained by aromatization of XIII by Dryden's procedure, which employs lithium, biphenyl, diphenylmethane, and tetrahydrofuran.[10]

Acetylation of alcohol IX with acetic anhydride and pyridine at room temperature provided the acetate X, which was converted into bromohydrin XII by Wettstein's method.[11] Bromohydrin XII may be regarded as a potential precursor of a C-19 functionalized derivative.[11,12]

SCHEME II



Experimental Section

Infrared spectra were determined in chloroform (unless otherwise noted) on a Model IR-5 Beckman infrared recording spectrophotometer. Ultraviolet absorption spectra were determined in ethanol (unless otherwise noted) on a Model DK-2A Beckman recording spectrophotometer. Nuclear magnetic resonance (nmr) spectra were determined on a Varian Associates A60 or A60A recording spectrometer in deuteriochloroform (unless otherwise noted), using tetramethylsilane as an internal reference. The optical rotatory dispersion was determined on a Cary Model 60 spectropolarimeter. Melting points were determined on a Fisher-Johns melting point apparatus and are corrected. Values of $[\alpha]$D in chloroform have been approximated to the nearest degree. The microanalyses were carried out by Mr. Joseph Alicino, Metuchen, N. J., and Spang Microanalytical Laboratory, Ann Arbor, Mich.

Δ^5-Etiojervene-3,11,17-trione 3,17-Diethylene Ketal (III).—A solution of Δ^4-etiojervene-3,11,17-trione (IV, 100 mg) in dry benzene was treated with ethylene glycol (2.0 ml) and *p*-toluenesulfonic acid monohydrate (11 mg) and the reaction mixture was refluxed for 21 hr in a flask fitted with a modified Dean–Stark apparatus. To the solution was added saturated sodium bicarbonate solution and water. The aqueous layer was washed with benzene and the organic layer was dried over magnesium sulfate. The benzene solution was evaporated under reduced pressure to yield a crystalline product, which was recrystallized from isopropyl ether to give needles (III, mp 206–207°, 90 mg, 70% yield). A sample was recrystallized from ether for analysis:

(8) For a recent review of the chemistry and stereochemistry of jervine, see S. M. Kupchan and A. W. By in "The Alkaloids," Vol. X, R. H. Manske, Ed., Academic Press Inc., New York, N. Y., 1967.

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(10) H. L. Dryden, G. M. Webber, and J. J. Wieczorek, *J. Am. Chem. Soc.*, **86**, 742 (1964).

(11) J. Kalvoda, K. Heusler, H. Ueberwasser, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **46**, 1361 (1963).

(12) H. Ueberwasser, K. Heusler, J. Kalvoda, Ch. Meystre, P. Wieland, G. Anner, and A. Wettstein, *ibid.*, **46**, 344 (1963).

mp 208–209°; $[\alpha]^{29}D$ −128° (*c* 0.48); λ_{max} 5.78, 8.78, 9.00, 9.26 μ.

Anal. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.19; H, 8.33.

Δ⁵-Etiojerven-11β-ol-3,17-dione 3,17-Diethylene Ketal (V).—To a solution of Δ⁵-etiojervene-3,11,17-trione 3,17-diethylene ketal (III, 421 mg) in ether (40 ml) at 47° was added with stirring a suspension of lithium aluminum hydride (89 mg) in ether (13 ml). After refluxing for 4 hr, the solution was cooled and 95% ethanol was added, followed by water. The aqueous layer was extracted with ether and the ether extracts were combined. The organic solution was then shaken successively with 4% hydrochloric acid, 5% sodium hydroxide, and water, and then dried over sodium sulfate. Evaporation of the ether under reduced pressure gave crystalline material which was recrystallized from ether to afford V (381 mg, mp 189–191°, 90% yield). A sample was recrystallized from ether for analysis: mp 195–196°; $[\alpha]^{36}D$ −6° (*c* 0.80); λ_{max} 2.75, 2.85, 8.50, 8.95, 9.25, 9.50 μ; nmr τ 4.73 (C-6, multiplet, 1 H), 6.05 (ketal, singlet, 8 H), 6.80 (C-11, multiplet, 1 H), 8.72 (C-19, singlet, 3 H), 9.00 (C-18, doublet, 3 H, J = 6.0 cps).

Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.88; H, 8.58.

Δ⁵-Etiojervene-11-chloro-3,17-dione 3,17-Diethylene Ketal (VI).—To Δ⁵-etiojerven-11β-ol-3,17-dione 3,17-diethylene ketal (V, 400 mg) in dry pyridine (2 ml) was added thionyl chloride (0.4 ml) and the mixture was left at room temperature for 25 min. To the solidified mass was added ice, ether, and 7% sodium hydroxide. The black aqueous layer was separated and extracted twice with ether. The yellow ether layers were combined and washed with 7% sodium hydroxide, 5% sulfuric acid, and water. The ether layer was evaporated to give the chloro compound VI (192 mg, 50% yield, mp 203–206° after crystallization from acetone). Further recrystallization from acetone gave a hygroscopic product: mp 211–212°; $[\alpha]^{22}D$ −10° (*c* 1.00); nmr τ 4.60 (C-6, multiplet, 1 H), 5.70 (C-11, multiplet, 1 H), 6.01 (ketal, singlet, 8 H), 8.95 (C-19, singlet, 3 H), 9.02 (C-18, doublet, 3 H, J = 6.5 cps); the infrared spectrum showed the absence of a hydroxyl peak.

Anal. Calcd for $C_{23}H_{33}O_4Cl$: C, 67.55; H, 8.36; Cl, 8.67. Found: C, 67.11; H, 8.15; Cl, 8.35.

Δ⁵-Etiojerven-3β-ol-11,17-dione 17-Monoethylene Ketal 3-Acetate (VII).—A solution of Δ⁵-etiojervene-11,17-dion-3β-ol 3-acetate (II, 12.67 g) in dry benzene (1.5 l.) was treated with ethylene glycol (230 ml). The mixture was refluxed with a Dean–Stark apparatus for 1 hr under magnetic stirring. To the hot reaction mixture was added *p*-toluenesulfonic acid monohydrate (1.39 g) and the solution was refluxed for 18.5 hr. To the cooled mixture was added saturated sodium bicarbonate solution and the aqueous layer was extracted twice with benzene. The organic layer was washed twice with water and dried over sodium sulfate. The benzene solution was evaporated under reduced pressure to give crystalline material which was recrystallized from chloroform–isopropyl ether to afford VII (needles, 10.70 g, mp 180–182°, 75% yield). Three recrystallizations from chloroform–isopropyl ether gave analytically pure VII: mp 191–192°; $[\alpha]^{28}D$ −147° (*c* 1.035); λ_{max} 5.80, 9.10, 9.25μ; nmr τ 4.57 (C-6, doublet, 1 H, J = 5 cps), 5.43 (C-3, multiplet, 1 H), 6.01 (ketal, singlet, 4 H), 7.96 (AcO, singlet, 3 H), 8.83 (C-18, doublet, 3 H, J = 6 cps), 8.95 (C-19, singlet, 3 H); benzene solution, 4.77 (J = 4.5 cps), 5.28, 6.42, 8.27, 8.51 (J = 5.5 cps), 9.08, respectively.

Anal. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.42; H, 7.95.

A minor impurity, Δ⁵-etiojerven-3β-ol-11,17-dione 17-monoethylene ketal (VIII), was isolated from crude VII by alumina chromatography. Recrystallization from benzene–Skellysolve C gave pure VIII: mp 165–167°; λ_{max}^{Nujol} 2.94, 5.79 μ; $[\alpha]^{27}D$ −157° (*c* 1.08); nmr τ 4.59 (C-6, doublet, 1 H, J = 5 cps), 6.02 (ketal, singlet, 4 H), 6.52 (C-3, multiplet, 1 H), 8.05 (HO, singlet, 1 H), 8.81 (C-18, doublet, 3 H, J = 5.5 cps), 8.97 (C-19, singlet, 3 H).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.84; H, 8.73.

Δ⁵-Etiojerven-3β-ol-17-one 17-Ethylene Ketal (IX).—A magnetically stirred solution of Δ⁵-etiojervene-11,17-dione 17-monoethylene ketal (VII, 4.92 g) in diethylene glycol (417 ml) containing potassium hydroxide (41.7 g) was heated at 140° for 4 hr. Hydrazine hydrate (99–100%, 32.2 ml) was added and the temperature was raised to 180° for 68 hr. The condenser was then removed for 1.5 hr and then replaced and the reaction mixture was heated at 195° for 3 hr. Ice was added to the cooled reaction mixture and the aqueous layer was extracted three times with ether (2 l.). The ether layer was washed with cold 5% hydrochloric acid and water and dried over sodium sulfate. The ether solution was evaporated under reduced pressure to give crystalline material which showed three spots upon thin layer chromatography.

This material was dissolved in benzene and applied to a column of Woelm neutral alumina (activity II, 65 g). Elution with benzene (2.4 l.) gave crystalline IX which was recrystallized from acetone–isopropyl ether to give prisms (1.46 g, mp 178–179°, 35% yield). Recrystallization from the same solvents gave pure IX: mp 178–179°; $[\alpha]^{29}D$ −29° (*c* 1.10); λ_{max} 2.92 μ.

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.70; H, 9.61.

Δ⁴-Etiojervene-3,17-dione 17-Monoethylene Ketal (XI).—To a mixture of dry toluene (250 ml) and cyclohexanone (8.34 ml) was added Δ⁵-etiojerven-3β-ol-17-one 17-ethylene ketal (IX, 1.23 g) and some toluene (83 ml) was distilled off. Aluminum isopropoxide (1.17 g) in toluene (83 ml) was added to the hot mixture and refluxed for 1.5 hr. To the cooled reaction mixture was added a saturated Rochelle salt solution (51 ml) and the mixture was steam distilled. The aqueous layer was extracted with chloroform and dried over sodium sulfate. Evaporation of the chloroform under reduced pressure gave an orange oil which crystallized on addition of isopropyl ether. Recrystallization from isopropyl ether gave needles of XI (889 mg, mp 141–142°, 72% yield). Further crystallization gave pure XI: mp 142–143°; $[\alpha]^{34}D$ +141° (δ 1.10); λ_{max} 238 mμ (ε 18,600); λ_{max} 6.02, 6.20, 9.03, 9.23 μ.

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.09; H, 9.12.

Δ¹,⁴-Etiojervadiene-3,17-dione 17-Monoethylene Ketal (XIII).—A solution of Δ⁴-etiojervene-3,17-dione 17-monoethylene ketal (XI, 600 mg) in dry distilled dioxane (12 ml) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (600 mg). After refluxing for 28 hr, the reaction was cooled and the precipitated quinol was filtered and washed thoroughly with chloroform. The filtrate was evaporated to dryness and the residue was taken up in benzene–ether (1:1). This was washed three times with saturated sodium sulfite solution and then with water. The organic layer was dried over sodium sulfate and evaporated to give an orange-brown oil which crystallized from acetone–isopropyl ether (366 mg, 62% yield). A sample was crystallized for analysis from the same solvents to give pure XIII: mp 168–169°; $[\alpha]^{32}D$ +91° (*c* 1.00); λ_{max} 243 mμ (ε 22,000); λ_{max} 6.03, 6.20, 6.40, 8.49, 8.90, 9.05, 9.25, 9.58 μ; nmr τ 3.15 (C-1, doublet, 1 H, J = 9.5 cps), 3.70 (C-2, doublet, 1 H, J = 1.5 cps), 3.85 (C-4, singlet, 1 H), 6.03 (ketal, singlet, 4 H), 8.84 (C-19, singlet, 3 H), 9.12 (C-18, doublet, 3 H, J = 5 cps).

Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.94; H, 8.52.

Δ¹,³,⁵(¹⁰)-Etiojervatrien-3-ol-17-one (XIV).—A mixture of biphenyl (240 mg), lithium dispersion (Lithium Corp. of America, Inc., 30% lithium, 68% paraffin, 2% oleic acid, 86 mg), and anhydrous tetrahydrofuran (1.5 ml) was refluxed under dry nitrogen for 15 min, when the solution became dark bluish green. Then diphenylmethane (0.15 ml) was added. A solution of XIII (294 mg) in anhydrous tetrahydrofuran (1 ml) was added over 15 min to the refluxing mixture. After refluxing for an additional 25 min, the excess lithium was decomposed with methanol (0.4 ml) and then water (0.4 ml) was added. After cooling, concentrated hydrochloric acid (0.6 ml) was added and the acidic solution was refluxed for 30 min. The solution was again cooled and water and benzene were added. The aqueous layer was extracted three more times with benzene and the combined organic layer was washed three times with water, dried over anhydrous sodium sulfate, filtered, and evaporated to give crude product (750 mg). The product was chromatographed on Brinkmann silica gel (30 g). Elution with benzene (200 ml) and chloroform–benzene (1:5, 100 ml; 1:3, 250 ml; 1:1, 360 ml), removed the wax, biphenyl, and diphenylmethane. Further elution with chloroform–benzene (1:1, 360 ml) gave Δ¹,³,⁵(¹⁰)-etiojervatrien-3-ol-17-one (XIV, 176 mg). Crystallization from methanol gave pure XIV (48 mg): mp 259.5–261° (vacuum capillary); λ_{max}^{KBr} 3.00, 5.93 μ; λ_{max} 282 mμ (ε 2,210); $\lambda_{max}^{0.2\%\ KOH-EtOH}$ 302 mμ (ε 1800), 242.5 mμ (ε 7600); nmr (d_5-pyridine) τ 2.98 (aryl H, singlet, 3 H), 8.88 (C-18, singlet, 3 H,

J = 6.5 cps); $[\phi]^{25}_{589}$ +141, $[\phi]^{25}_{365}$ 0, $[\phi]^{25}_{310}$ −3800, $[\phi]^{25}_{296}$ 0, $[\phi]^{25}_{270}$ +8460, $[\phi]^{25}_{240}$ +10,600 (*c* 0.16, 95% ethanol).

Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.01; H, 8.29.

A second crop (45 mg, mp 257–259°) was obtained from methanol–benzene. Final elution of column with methanol–chloroform (1:10) yielded polar impurity (85 mg).

Δ^5-Etiojerven-3β-ol-17-one 17-Ethylene Ketal 3-Acetate (X).—A solution of Δ^5-etiojerven-3β-ol-17-one 17-ethylene ketal (IX, 3.52 g) in pyridine (47.0 ml) and acetic anhydride (47.0 ml) was left to stand at room temperature for 19.5 hr. The reaction mixture was added slowly to a mixture of ice, 2 *N* sodium carbonate solution, and chloroform. The aqueous layer was extracted twice with chloroform and the organic layer was then washed with 2 *N* sodium carbonate solution and water (three times). After drying over sodium sulfate, the chloroform was evaporated under reduced pressure to give a glassy residue. The residue was repeatedly treated with benzene and the benzene solutions evaporated. The resulting crystalline material was recrystallized from isopropyl ether to give prisms of X (3.89 g, mp 146–147°, 98% yield). A sample was recrystallized from ether: mp 147–148°; $[\alpha]^{27}D$ −32° (*c* 1.00); λ_{max} 5.80, 8.00 μ; nmr τ 4.62 (C-6, multiplet, 1 H), 5.40 (C-3, multiplet, 1 H), 6.03 (ketal, singlet, 4 H), 7.97 (AcO, singlet, 3 H), 9.02 (C-19, singlet, 3 H), 9.15 (C-18, doublet, 3 H, J = 5.5 cps); benzene solution, 4.67 (J = 5 cps), 5.22, 6.37, 8.23, 9.17, 8.97 (J = 5 cps), respectively.

Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.65; H, 9.11.

Etiojervane-5α-bromo-3β,6β-diol-17-one 17-Ethylene Ketal 3-Acetate (XII).—A mixture of Δ^5-etiojerven-3β-ol-17-one 17-ethylene ketal 3-acetate (X, 500 mg) and N-bromoacetamide (250 mg) in ether (12 ml), water (0.55 ml), and 60% perchloric acid (0.1 ml) was stirred in the dark at 22° for 15 min and then at room temperature for 40 min. The mixture was then diluted with ether and 1% sodium thiosulfate (50 ml). The aqueous layer was extracted once more with ether and the combined organic layers were washed with saturated sodium bicarbonate and water (twice). The ether layer was dried over sodium sulfate and evaporated to give a crystalline residue, which was recrystallized from ether to give the bromohydrin XII (206 mg, mp 154–155°). A sample was recrystallized from ether three times to give pure XII: mp 159–160°; $[\alpha]^{25}D$ −24° (*c* 1.10); λ_{max} 2.80, 2.90, 5.80, 8.00 μ; nmr τ 4.48 (C-3, multiplet, 1 H), 5.70 (C-6, multiplet, 1 H), 6.08 (ketal, singlet, 4 H), 7.70 (HO, singlet, 1 H), 7.98 (AcO, singlet, 3 H), 8.70 (C-19, singlet, 3 H), 9.16 (C-18, doublet, 3 H, J = 6 cps).

Anal. Calcd for $C_{23}H_{35}O_5Br$: C, 58.59; H, 7.48; Br, 16.96. Found: C, 58.60; H, 7.49; Br, 16.79.

Registry No.—III, 15314-12-2; V, 15296-93-2; VI, 15352-73-5; VII, 15296-94-3; VIII, 15314-13-3; IX, 15314-14-4; X, 15296-95-4; XI, 15314-15-5; XII, 15296-96-5; XIII, 15296-97-6; XIV, 15296-98-7.

A Study of the Ozonolysis of the Cross-Conjugated Steroidal $\Delta^{1,4}$-3-Ketone System[1]

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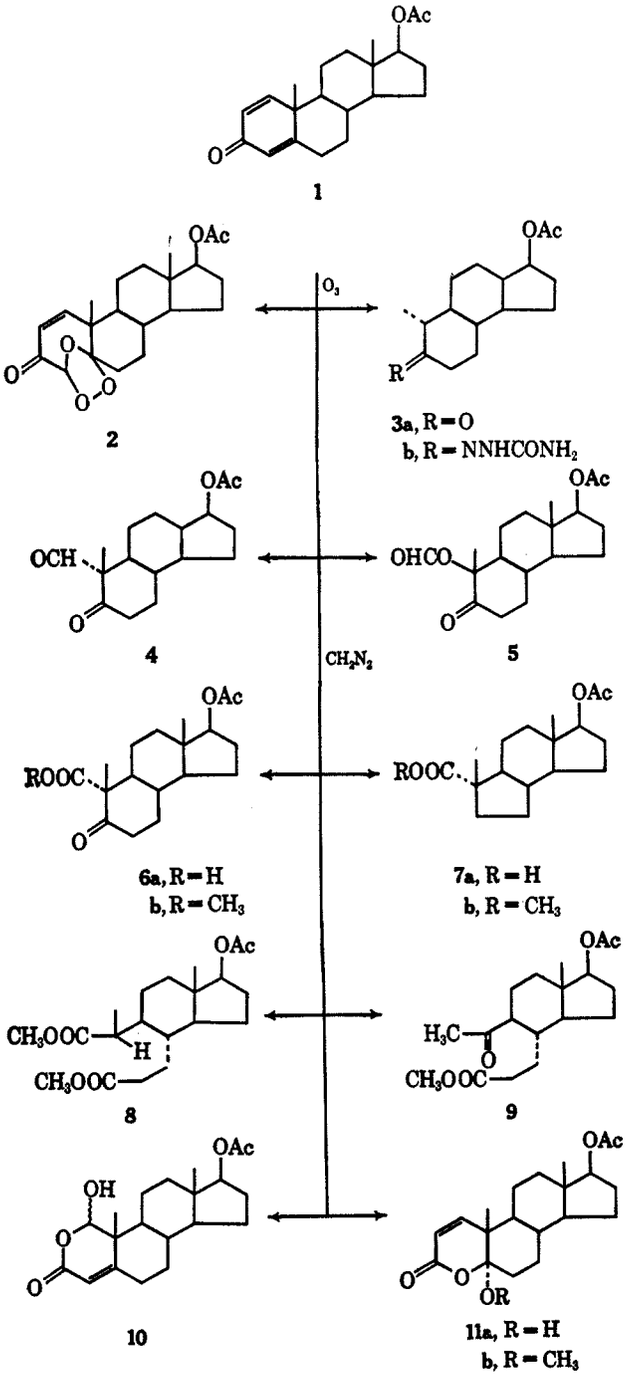
Several years ago, Caspi and co-workers[3] reported the results of their studies concerned with the ozonolysis of several steroidal $\Delta^{1,4}$-3-ketones. In essence these workers found that the nature and amounts of products formed are highly dependent on the structure of the starting material and also on the reaction conditions employed. As part of a program designed to yield steroids containing heteroatoms in their skeletal ring systems, we investigated the ozonolytic cleavage of 1-dehydrotestosterone acetate (1) to determine the feasibility of using such a method to effect a synthetically useful degradation of ring A. Unfortunately, our ozonation efforts consistently led to complex mixtures of products under the conditions tried, the results largely running parallel with those reported earlier.[3] For example, when an ethyl acetate solution of 1-dehydrotestosterone acetate (1) was treated with ozone for 6 hr and worked up in the normal fashion, compounds **2**, **3a**, **4**, and **5** were isolated from the neutral fraction, while the acidic portion (after esterification) yielded the esters **6b**, **7b**, **8**, and **9**. Compounds



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(2) Postdoctoral Research Associate, 1965–1967.

(3) (a) E. Caspi, W. Schmid, and B. T. Khan, *Tetrahedron*, **18**, 767 (1962); (b) E. Caspi, B. T. Khan, and S. N. Balasubrahmanyam, *ibid.*, 1013 (1962); (c) S. N. Balasubrahmanyam, E. Caspi, and B. T. Khan, *J. Chem. Soc.*, 761 (1963).