[CONTRIBUTION FROM THE LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY]

$\Delta^{5,7}$-STEROIDS. XVI. STEROIDAL CYCLIC KETALS. VI.[1,2] THE PREPARATION AND TRANSFORMATION PRODUCTS OF $\Delta^{5,7}$-22a-SPIROSTADIENE-3-ONE-ETHYLENE KETAL

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In previous papers of this series (1) there was presented definitive evidence in confirmation of the remarkable observation of Fernholz and Stavely (2), that when a Δ^4-3-ketosteroid is treated with ethylene glycol, the resulting ketal is formed with coincident rearrangement of the double bond to the C-5,6 position.[3] Our work showed that the ethylene ketal of a Δ^4-3-ketosteroid on reaction with NBS (N-bromosuccinimide) followed by dehydrobromination resulted in the formation of a $\Delta^{5,7}$-steroid. Moreover, it was demonstrated that a $\Delta^{4,7}$-3-ketosteroid on ketalization was converted into a $\Delta^{5,7}$-ketal.

The purpose of this paper is to present the results obtained on application of these ketal transformations to the sapogenin type of molecule.

Treatment of Δ^4-22a-spirostene-3-one (Δ^4-dehydrotigogenone) (I) (Flowsheet I) with ethylene glycol (benzene, *p*-toluenesulfonic acid) gave in 68% yield the ethylene ketal (IIa). A similar reaction with 2,2-dimethyl-1,3-propanediol resulted in the corresponding ketal (IIb). The ketone (I) was regenerated from the ketal (IIa) by hydrolysis of the latter with aqueous acetic acid (76% yield).

The Δ^5-ketal (IIa), when submitted to the NBS reaction followed by dehydrobromination with *s*-collidine in xylene, was converted into the desired $\Delta^{5,7}$-22a-spirostadiene-3-one-ethylene ketal (III) (65% spectroscopic yield). Pure III was obtained in 52% yield. This preparation was performed by utilizing a procedure slightly modified from that conventionally employed in this laboratory (3). This yield probably constituted the highest ever obtained in the conversion of a Δ^5- to a $\Delta^{5,7}$-steroid. As stated previously (1a), the ethylene ketal group at C-3 apparently hinders the usual allylic shift associated with the formation of a $\Delta^{5,7}$-steroid by the NBS method; *i.e*, the formation of a $\Delta^{4,6}$-steroid. This observation finds support from the results of an exhaustive investigation of the products formed in the preparation of the $\Delta^{5,7}$-ketal (III) from the Δ^5-ketal (IIa). Other than the $\Delta^{5,7}$-ketal (III) only one additional product was isolated, namely, $\Delta^{4,6}$-22a-spirostadiene-3-one (IV). *No* $\Delta^{4,6}$-22a-spirostadiene-3-one-ethylene ketal was obtained, or even, decisively indicated spectroscopically in any of the numerous fractions isolated. The formation of the $\Delta^{4,6}$-3-one (IV) may be attributed to trace hydrolysis of the ketal starting

[1] (a) Paper XV, Bernstein, Heller, and Williams, *J. Am. Chem. Soc.*,**75**, 1480 (1953); (b) Paper V, Bernstein, Lenhard, and Williams, *J. Org. Chem.*, **18**, 1166 (1953).

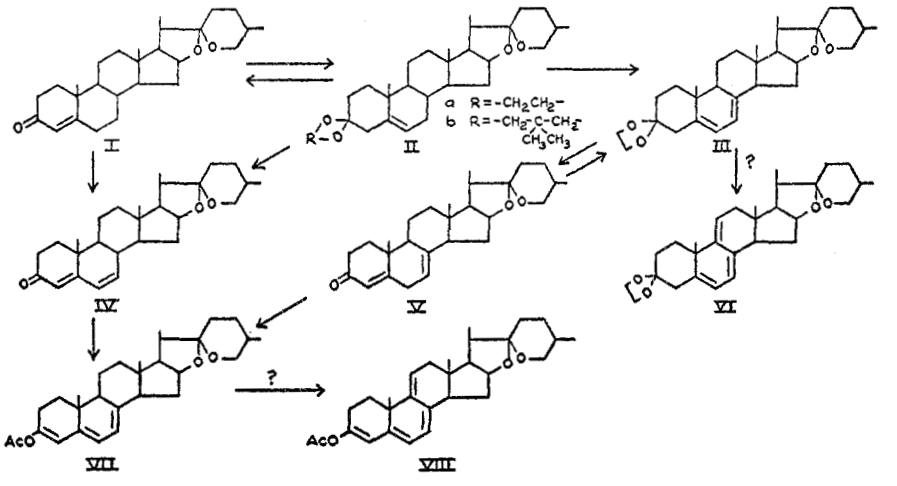
[2] Presented in part before the Organic Group at the Fourth Annual Meeting of the New York Section, American Chemical Society, New York, N. Y., February 8, 1952.

[3] Recently, Poos, Arth, Beyler, and Sarett [*J. Am. Chem. Soc.*, **75**, 422 (1953)] have presented additional chemical evidence for the migration of the double bond.

material prior to bromination and dehydrobromination.[4] The preparation of the $\Delta^{4,6}$-3-one (IV) directly from the Δ^{4}-3-one (I) has been reported by Romo, Ringold, Rosenkranz, and Djerassi (4). We have successfully repeated this preparation, but find minor discrepancies in the characterization of IV, especially in regard to its ultraviolet absorption spectrum.

The $\Delta^{5,7}$-ketal (III) on aqueous acetic acid hydrolysis was converted into $\Delta^{4,7}$-22a-spirostadiene-3-one (V), and *not* into the $\Delta^{4,6}$-3-one (IV). Ketalization of the $\Delta^{4,7}$-3-one (V) gave back the $\Delta^{5,7}$-ketal (III). These findings were in accord with our previous experience with such transformations (1).

FLOWSHEET I



The $\Delta^{5,7}$-ketal (III) in chloroform was subjected to dehydrogenation with mercuric acetate in glacial acetic acid, and the $\Delta^{5,7,9(11)}$-22a-spirostatriene-3-one-ethylene ketal (VI) was obtained in 11% yield. The assigned structure of the latter was supported by its ultraviolet absorption spectrum, λ_{max} 312–315 (inflection), 324–325, and 337–338 mμ ($\epsilon_{324-325}$ 11,500) (5), and also by its highly positive optical rotation (5, 6). Unfortunately, however, this preparation has given irregular results. We have not succeeded in repeating the isolation of a pure product.

Acetylation of $\Delta^{4,6}$-22a-spirostadiene-3-one (IV) with acetic anhydride and acetyl chloride gave in 26% yield $\Delta^{3,5,7}$-22a-spirostatriene-3-ol-acetate (VII) (7, footnote 1a). The latter was obtained also from the $\Delta^{4,7}$-3-ketone (V) with acetic anhydride and pyridine in the manner described by others (8).

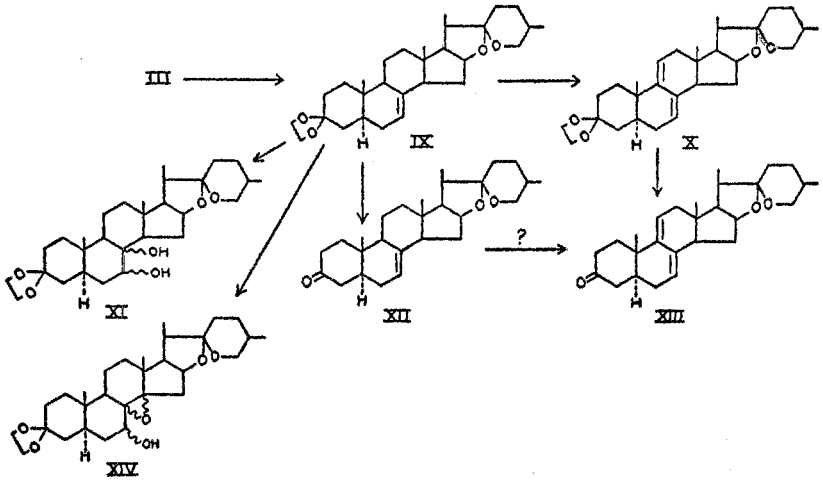
In a recent paper (7b), it was demonstrated that a $\Delta^{3,5,7}$-enol-acetate may be dehydrogenated successfully with mercuric acetate in acetic acid to afford the corresponding $\Delta^{3,5,7,9(11)}$-enol acetate. The $\Delta^{3,5,7}$-enol acetate (VII) was converted accordingly into the known $\Delta^{3,5,7,9(11)}$-enol acetate (VIII), previously described

[4] During the development of the procedure for the preparation of the $\Delta^{5,7}$-ketal (III) from the Δ^{5}-ketal (IIa), one run gave predominantly the $\Delta^{4,6}$-3-one (IV) rather than the $\Delta^{5,7}$-ketal (III).

by the Syntex group (7). The physical constants for VIII described by both groups are in good agreement except for the ultraviolet absorption spectrum. Here, also, we regret to state that, for some inexplicable reason, the preparation is not reproducible.

Δ^7-22a-Allospirostene-3-one-ethylene ketal (IX) (Flowsheet II) was obtained in 84% yield from the $\Delta^{5,7}$-ketal (III) by hydrogenation of the latter in absolute alcohol-ether with a W-2 Raney nickel catalyst. Removal of the ketal group with aqueous acetic acid afforded Δ^7-22a-allospirostene-3-one (XII).

FLOWSHEET II



The Δ^7-ketal (IX) on dehydrogenation with mercuric acetate in glacial acetic acid was converted into the $\Delta^{7,9(11)}$-ketal (X) (25% yield). Aqueous acetic acid hydrolysis led to $\Delta^{7,9(11)}$-22a-allospirostadiene-3-one (XIII). An attempt to prepare the latter directly from XII with mercuric acetate resulted in a product, most probably impure XIII.

The Δ^7-ketal (IX) was hydroxylated with osmium tetroxide and the diol (XI) was obtained in 5.5% yield. The configurations of the hydroxyl groups are uncertain.

Treatment of the Δ^7-ketal (IX) with peroxybenzoic acid introduced two oxygens into the molecule, one in the form of an hydroxyl group, and the other, presumably, in the form of an oxido bridge. The structure (XIV) indicated is based on the work of others (9). The possibility exists that the oxido bridge may be at the C-8,9 position rather than as shown in XIV. Some basis for this supposition may be deduced from the work of Heusser, and co-workers (10) who found that chromic acid oxidation of a Δ^7-steroid gave rise to two compounds, namely, 8,9-oxido-, and 8,14-oxido-7-ketosteroid.

The presence of an hydroxyl group in XIV was shown by acetylation under mild conditions. Although the reaction product was incompletely characterized, the presence of the acetate group was confirmed by infrared analysis. Treatment

of XIV with lithium aluminum hydride or potassium hydroxide in methanol did not alter the molecule.

It has been demonstrated (11) that certain ketals showed abnormal behavior in a rotational analysis. We would like to point out another such instance. It has been considered that *generally* a $\Delta^{5,7}$-steroid has a more negative optical rotation than the corresponding Δ^{5}-steroid (12). A number of Δ^{5}- and $\Delta^{5,7}$-ketals have been prepared during the course of this series of papers, and the rotations of these compounds are listed in Table I. An examination of the rotations of

TABLE I

OPTICAL ROTATIONS OF Δ^{5}- AND $\Delta^{5,7}$-KETALS

COMPOUND	$[\alpha]_D$ ($CHCl_3$)	REFERENCE
[1] Δ^{5}-Cholestene-3-one-ethylene ketal	−31°	1a
$\Delta^{5,7}$-Cholestadiene-3-one-ethylene ketal	−14°, −17°	1a
[2] Δ^{5}-22a-Spirostene-3-one-ethylene ketal	−98°	This work
$\Delta^{5,7}$-22a-Spirostadiene-3-one-ethylene ketal	−73°	This work
[3] Δ^{5}-Pregnene-3,20-dione-di-ethylene ketal	−29°	1b
$\Delta^{5,7}$-Pregnadiene-3,20-dione-di-ethylene ketal	−12°	1b
[4] Δ^{5}-Pregnene-21-ol-3,20-dione-21-acetate-3-ethylene ketal	+43°	1b
$\Delta^{5,7}$-Pregnadiene-21-ol-3,20-dione-21-acetate-3-ethylene ketal	+56°	1b
[5] Δ^{5}-Androstene-17β-ol-3-one-17-acetate-3-ethylene ketal	−52°	1a
$\Delta^{5,7}$-Androstadiene-17β-ol-3-one-17-acetate-3-ethylene ketal	−72°	1a
[6] Δ^{5}-Androstene-17β-ol-3-one-17-benzoate-3-ethylene ketal	+15°	1a
$\Delta^{5,7}$-Androstadiene-17β-ol-3-one-17-benzoate-3-ethylene ketal	+15°, +18°	1a

six pairs of compounds reveals that the opposite correlation may be true for such compounds, *i.e.*, the Δ^{5}-ketal will have a more negative rotation. The "testosterone" compounds may be considered exceptional, ascribable to C-17 vicinal action.

Finally, we wish to record an interesting observation concerning the ultraviolet absorption spectra of $\Delta^{4,7}$-22a-spirostadiene-3-one (V), and, in general, of $\Delta^{4,7}$-3-ketosteroids. L. Dorfman (13), in an extensive study of the correlation of ultraviolet absorption spectra and structure of steroids, has observed certain generalizations concerning the λ_{max} of Δ^{4}-3-ketosteroids.[5] Thus, the λ_{max} of Δ^{4}-3-ketosteroids (generally at about 240–241 mμ in alcohol) may be influenced by the presence of an isolated chromophore, such as a double bond. A C-7,8 double bond produces an hypsochromic effect of about 3 mμ, and accordingly,

[5] A generalization concerning the λ_{max} of 11-oxygenated-Δ^{4}-3-ketosteroids has been proposed by Dorfman, and, independently, by this group (11).

$\Delta^{4,7}$-3-ketosteroids will exhibit a maximum at about 237–238 mμ. $\Delta^{4,7}$-22a-spirostadiene-3-one (V) exhibits a maximum at 237–239 mμ, which is in accord with Dorfman's generalization.

EXPERIMENTAL

Melting points. All m.p.'s are uncorrected, and were determined with uncalibrated Anschütz thermometers.

Absorption spectra. All spectra were determined in absolute alcohol with a Beckman quartz spectrophotometer (Model DU).

Optical rotations. The sample was dissolved in chloroform to make a 2-ml. solution, and the rotation was determined in a 1-dm. semi-micro tube at the wavelength 5893 Å (D), and in some cases, also at 5461 Å (Hg).

Petroleum ether. The fraction used boiled at 64–66°, and was purified with potassium permanganate and conc'd sulfuric acid.

Δ^5-*22a-Spirostene-3-one-ethylene ketal* (IIa). A mixture of I (2 g.), toluene (80 ml.), ethylene glycol (10 ml.), and *p*-toluenesulfonic acid monohydrate (60 mg.) was reacted in the same manner as described in a previous publication (1a) (reflux 4 hours); 1.5 g. of IIa; m.p. 235.5–239° (from acetone-methanol); no selective absorption in u.v., $[\alpha]_D^{29}$ −98°, $[\alpha]_{Hg}^{29}$ −115° (22 mg., α_D −1.08°, α_{Hg} −1.27°), α_{Hg}/α_D 1.17, $[M]_D$ −448; 68% yield.

Anal. Calc'd for $C_{29}H_{44}O_4$ (456.64): C, 76.27; H 9.71.

Found: C, 76.30; H 9.53.

Δ^5-*22a-Spirostene-3-one-(2',2'-dimethyl)trimethylene ketal* (IIb). A mixture of I (3 g.), 2,2-dimethyl-1,3-propanediol (1.15 g.) toluene (120 ml.), and *p*-toluenesulfonic acid (90 mg.) was reacted in the manner described for IIa (reflux 3 hours); 1.23 g. of IIb; m.p. 230–232° (from ether-acetone-methanol); no selective absorption in u.v., $[\alpha]_D^{27}$ −99° (24.9 mg., α_D −1.23°); $[M]_D$ −493; 34% yield.

Anal. Calc'd for $C_{32}H_{50}O_4$ (498.72): C, 77.06; H, 10.11.

Found: C, 77.19; H, 10.39.

Δ^4-*22a-Spirostene-3-one.* (I). Compound IIa (1.5 g.) dissolved in 60 ml. of glacial acetic acid was treated with 30 ml. of 50% aqueous acetic acid. The solution was heated on the steam-bath for ¾ hour, when water was added. The mixture was cooled, and the crystals were collected, and washed with water, and a small amount of methanol; 1.03 g., m.p. 190–192°; λ_{max} 241 mμ, ε 16,700; 76% yield.

$\Delta^{5,7}$-*22a-Spirostadiene-3-one-ethylene ketal* (III). *A.* To a mixture of carbon tetrachloride (30 ml.) (dried over potassium carbonate), and petroleum ether (45 ml.) (dried over sodium) was added anhydrous potassium carbonate (0.5 g.), Δ^5-22a-spirostene-3-one-ethylene ketal (IIa) (2.0 g., 0.0044 mole), and NBS (975 mg. 0.0055 mole). The mixture was refluxed and irradiated for 4 minutes by the heat and light of a photospot lamp (type RSP-2, General Electric Company). *s*-Collidine (2 ml.) was added, and the mixture was cooled, and filtered with the aid of carbon tetrachloride. The filtrate was evaporated *in vacuo* at room temperature and below. The residue was treated with xylene (75 ml.) and *s*-collidine (6 ml.); the mixture was refluxed for 45 minutes, cooled, and filtered. The filtrate was steam-distilled for 2 hours, and the residue was extracted with ether. The washed and dried extract was evaporated *in vacuo*. The residue was crystallized from ether-acetone-methanol to afford 920 mg. (fraction *a*), m.p. 205–212°, ϵ_{271} 10,000; ϵ_{282} 10,500; ϵ_{293} 6,200. The mother liquor on concentration (acetone-methanol) yielded three additional fractions (in order of increasing solubility): *b*, 480 mg., m.p. 195°, unsharp, ϵ_{271} 9,800; $\epsilon_{281-282}$ 10,500; ϵ_{293} 6,200; *c*, 50 mg., m.p. 180–190°, ϵ_{271} 8,200; $\epsilon_{281-282}$ 9,000; $\epsilon_{293-294}$ 5,600; and, *d*, 300 mg., m.p. 100–135° d., ϵ_{241} 4,150 (inflection); ϵ_{282} 11,200; ϵ_{322} 1,100. The material in fractions *a*, *b*, and *c* constituted a 65% "spectroscopic" yield of III, based on ϵ_{282} 11,700.

Fraction *a* on recrystallization from acetone-methanol gave 830 mg. of pure III; m.p. 215–218°; ϵ_{271} 11,200; ϵ_{281} 11,800; ϵ_{293} 6,900; $[\alpha]_D^{30}$ −73° (28.8 mg., α_D −1.05°).

Anal. Calc'd for $C_{29}H_{42}O_4$ (454.63): C, 76.61; H, 9.31.

Found: C, 76.69; H, 9.29.

The mother liquor was combined with fractions *b*, *c*, and *d*, and the mixture was triangularly recrystallized from acetone-methanol. This resulted in the following fractions (in order of increasing solubility): 200 mg., m.p. 216–220°, ϵ_{271} 11,000; $\epsilon_{281-282}$ 11,700; ϵ_{293} 6,800; 70 mg., m.p. 219–221°, ϵ_{271} 9,100; ϵ_{281} 9,500; ϵ_{293} 5,500; and 20 mg., m.p. 194–200°, $\epsilon_{283-284}$ 23,000; ϵ_{320} 1,100.

The over-all weight of pure $\Delta^{5,7}$-ketal (III) was 1.03 g., 52% yield.

B. A mixture of the $\Delta^{4,7}$-3-ketone (V) (5 g.), toluene (200 ml.), ethylene glycol (25 ml.), and *p*-toluenesulfonic acid monohydrate (150 mg.) was reacted in the manner described for IIa (reflux 5 hours); 2.0 g., m.p. 216–218.5° (from ether-acetone-methanol); ϵ_{271} 10,800; ϵ_{282} 11,300; ϵ_{293} 6,600.

$\Delta^{4,6}$-*22a-Spirostadiene-3-one* (IV). The Δ^4-3-ketone (I) was brominated and dehydrobrominated essentially by the method of Romo and coworkers (4): m.p. 212–213° (from acetone-methanol); λ_{max} 282–286 mμ, ϵ 23,900; $[\alpha]_D^{29}$ −64° (39.6 mg., α_D −1.27°). Literature (4) m.p. 205–207°; $[\alpha]_D^{20}$ −55° ($CHCl_3$), $\lambda_{max}^{alc.}$ 284 mμ, ϵ 28,100; (14) m.p. 205–207°.

$\Delta^{4,7}$-*22a-Spirostadiene-3-one* (V). To a warm solution of the $\Delta^{5,7}$-ketal (III) (1 g.) in glacial acetic acid (35 ml.) was added a few drops of water, followed by 50% (v./v.) acetic acid (20 ml.). The mixture was heated on the steam-bath for ½ hour. Addition of water, and cooling afforded yellow crystals, m.p. 168–171°. Recrystallization from acetone-water gave 740 mg. of pure V (slight yellow coloration); m.p. 187–189°; λ_{max} 237–239 mμ, ϵ 15,300; $[\alpha]_D^{21}$ −60°, $[\alpha]_{Hg}^{21}$ −75° (14.1 mg., α_D −0.42°, α_{Hg} −0.53°) α_{Hg}/α_D 1.26; $[M]_D$ −240; 82% yield. Literature (8); m.p. 188–190° (Kofler), $\lambda_{max}^{alc.}$ 238 mμ, ϵ 19,500; $[\alpha]_D^{20}$ −65° ($CHCl_3$).

$\Delta^{5,7,9(11)}$-*22a-Spirostatriene-3-one-ethylene ketal* (VI). The $\Delta^{5,7}$-ketal (III) (1 g.) in chloroform (35 ml.) was treated with mercuric acetate (2.6 g.) in glacial acetic acid (50 ml.). The mixture was shaken at room temperature for 22 hours, when it was added cautiously to a sodium bicarbonate solution. The chloroform layer was separated, washed with water, dried, and evaporated *in vacuo*. The residue was crystallized from acetone-ether; fraction *a*: 0.32 g., yellow powder; m.p. 162–200° d., unsharp, λ_{max} 235, 312–313 (inflection), 328–329 (inflection), and 350–355 mμ. From the mother liquor by successive concentrations there were obtained the following: fraction *b*: 0.2 g. yellow, m.p. 177–185° d., $\epsilon_{323-325}$ 11,300; fraction *c*: 0.17 g., m.p. 169–185° d., λ_{max} 343–345 mμ; and fraction *d*: 40 mg., light yellow, m.p. 173–177°, $\epsilon_{324-326}$ 12,200. Recrystallization of fractions *b* and *d* combined from acetone-methanol, and methanol gave 110 mg., m.p. 183–187°, λ_{max} 312–315 (inflection), 324–325, and 337–338 mμ, ϵ 10,100; 11,500; and 7,200; respectively; $[\alpha]_D^{24}$ +210° (15.1 mg., α_D +1.58°); $[M]_D$ +949; 11% yield.

Anal. Calc'd for $C_{29}H_{40}O_4$ (452.61): C, 76.95; H, 8.91.

Found: C, 77.27; H, 9.12.

$\Delta^{3,5,7}$-*22a-Spirostatriene-3-ol-acetate* (VII). *A*. A solution of 450 mg. of the $\Delta^{4,6}$-3-one (IV) in 5 ml. of acetic anhydride, and 5 ml. of acetyl chloride was refluxed for 4 hours. The residue obtained on evaporation *in vacuo* was crystallized from methanol (Norit treatment); 200 mg., m.p. 179–182°. Three crystallizations from methanol gave 130 mg. of pure VII; m.p. 193–195°; λ_{max} 303, 315, and 330 mμ, ϵ 18,500; 23,000; and 16,500; respectively; $[\alpha]_D^{28}$ −169°, $[\alpha]_{Hg}^{28}$ −209° (20 mg., α_D −169°, α_{Hg} −2.09°) α_{Hg}/α_D 1.23., $[M]_D$ −761; 26% yield. Literature (8): m.p. 188–190° (Kofler); $[\alpha]_D^{20}$ −163° ($CHCl_3$); $\epsilon_{302}^{alc.}$ 20,000; ϵ_{314} 23,400; and ϵ_{330} 17,400.

B. Treatment of the $\Delta^{4,7}$-3-ketone (V) with acetic anhydride and pyridine afforded VII; m.p. 193–195°; ϵ_{302} 19,200; ϵ_{315} 23,200; and ϵ_{330} 17,400.

$\Delta^{3,5,7,9(11)}$-*22a-Spirostatetraene-3-ol-acetate* (VIII). A mixture of the $\Delta^{3,5,7}$-enol-acetate (VII) (0.91 g.) in chloroform (15 ml.), and mercuric acetate (1.8 g.) in glacial acetic acid (25 ml.) was reacted in the manner described above. The chloroform extract was evaporated *in vacuo*, and the residue was crystallized from ethyl acetate, followed by recrystallization from acetone-methanol; 0.12 g. (pale yellow); m.p. 176–178° with previous softening at 174°; λ_{max} 335, 355–356, and 374–375 mμ; ϵ 13,600; 15,600; and 11,500; respectively; $[\alpha]_D^{30}$ −208° (16.8 mg., α_D −1.75°); $[M]_D$ −936; 13% yield. Literature (8): m.p. 175–176° (Kofler); $\epsilon_{336}^{alc.}$ 17,800; ϵ_{354} 21,900; ϵ_{372} 16,200; $[\alpha]_D^{20}$ −223° ($CHCl_3$).

Anal. Calc'd for $C_{29}H_{38}O_4$ (450.59): C, 77.30; H, 8.50.

Found: C, 77.04; H, 8.67.

Δ^{7}-*22a-Allospirostene-3-one-ethylene ketal* (IX). The $\Delta^{5,7}$-ketal (III) (0.45 g.) in 25% (v./v.) absolute alcohol-ether (200 ml.) was shaken for 1¼ hours with W2 Raney nickel catalyst (ca. 1 g.) in a hydrogen atmosphere (26°, atm. press.). The catalyst was removed by filtration, and the filtrate was evaporated *in vacuo*. Recrystallization of the residue from acetone-methanol gave IX, 388 mg. (86% yield); m.p. 229–233°. Further recrystallization gave pure IX; 220 mg., m.p. 231–236°; $[\alpha]_D^{30}$ −68°, $[\alpha]_{Hg}^{30}$ −84° (26.8 mg., α_D −0.91°, α_{Hg} −1.12°) α_{Hg}/α_D 1.23, $[M]_D$ −310.

Anal. Calc'd for $C_{29}H_{44}O_4$ (456.64): C, 76.27; H, 9.71.
Found: C, 76.33; H, 9.65.

$\Delta^{7,9(11)}$-*22a-Allospirostadiene-3-one-ethylene ketal* (X). To the Δ^{7}-ketal (IX) (1 g.) in chloroform (35 ml.) was added mercuric acetate (2.6 g.) in glacial acetic acid (50 ml.). The mixture was shaken for 24 hours at room temperature, and was filtered. The filtrate was added cautiously to a sodium bicarbonate solution, and the product was extracted with carbon tetrachloride. The extract was washed, dried, and evaporated *in vacuo*. The residue was crystallized from ether-methanol; 500 mg., m.p. 195–207°; ϵ_{243} 10,400. Several recrystallizations from ether-methanol gave 250 mg. of pure X; m.p. 216–219°; λ_{max} 236, 243, and 250 mμ, ϵ 14,900; 16,700; and 11,000; respectively; $[\alpha]_D^{29}$ ±0° (22 mg., α_D −0.02°); $[M]_D$ ±0; 25% yield.

Anal. Calc'd for $C_{29}H_{42}O_4$ (454.63): C, 76.61; H, 9.31.
Found: C, 76.44; H, 9.32.

22a-Allospirostane-7ξ,8ξ-diol-3-one-ethylene ketal (XI). A solution of IX (1.62 g.) in benzene (14.5 ml.) was treated with pyridine (1.1 g.) and osmium tetroxide (0.97 g.), and was allowed to stand at room temperature for 7 days. The residue, obtained on evaporation *in vacuo*, in ethanol (55 ml.) was refluxed for 1½ hours with sodium sulfite (8 g.) in water (40 ml.). The hot mixture was filtered through Celite, and evaporated *in vacuo*. The residue was dissolved in methanol to give an opalescent solution which was clarified by filtration through Celite. Concentration of the filtrate with simultaneous addition of methanol gave 220 mg., m.p. 262–264°. Pure XI was obtained after several recrystallizations from methanol; m.p. 277–279°; $[\alpha]_D^{30}$ −115° (16 mg., α_D −0.92°); $[M]_D$ −564; 5.5% yield.

Anal. Calc'd for $C_{29}H_{46}O_6$ (490.66): C, 70.98; H, 9.45.
Found: C, 71.10; H, 9.26.

Δ^{7}-*22a-Allospirostene-3-one* (XII). To a solution of IX (0.5 g.) in glacial acetic acid (45 ml.) was added water (5 ml.); the mixture was heated on the steam-bath for 20 minutes after complete solution. Water was added to the hot solution which on being cooled gave crystals; 430 mg., m.p. 230–233°. Two recrystallizations from acetone-methanol resulted in pure XII; 320 mg., m.p. 235–237°. Admixture m.p. determination with starting material (IX) showed a marked depression; $[\alpha]_D^{24}$ −65°, $[\alpha]_{Hg}^{24}$ −77° (23.7 mg., α_D −0.77°, α_{Hg} −0.91°) α_{Hg}/α_D 1.18, $[M]_D$ −268; 71% yield.

Anal. Calc'd for $C_{27}H_{40}O_3$ (412.59): C, 78.59; H, 9.77.
Found: C, 78.31; H, 9.81.

$\Delta^{7,9(11)}$-*22a-Allospirostadiene-3-one* (XIII). *A.* The $\Delta^{7,9(11)}$-ketal (X) (110 mg.) was dissolved by heating in 10 ml. of glacial acetic acid. Water (1 ml.) was added, and the solution was heated on the steam-bath for about ½ hour, when additional water was added. The mixture was cooled, and the crystals were collected, and washed with water followed by a small amount of methanol; 80 mg., m.p. 213–216° with previous softening. Two recrystallizations from acetone-water gave pure XIII; 47 mg., m.p. 211–216°, with previous softening at 207°; λ_{max} 236, 243, and 251 mμ, ϵ 15,000; 16,600; and 11,000; respectively; $[\alpha]_D^{23}$ +16° (15.8 mg., α_D + 0.13°); $[M]_D$ +66; 47% yield.

Anal. Calc'd for $C_{27}H_{38}O_3$ (410.57): C, 78.98; H, 9.33.
Found: C, 78.98; H, 9.43.

B. A solution of the Δ^{7}-3-ketone (XII) (0.2 g.) in chloroform (6.5 ml.) was treated with a solution of mercuric acetate (0.54 g.) in glacial acetic acid (10 ml.). The mixture was shaken at room temperature for 40 hours. Additional chloroform was added, and the mixture was filtered. The filtrate was transferred to a separatory-funnel, and the chloroform solution

was washed with water, saturated sodium bicarbonate solution, and water. The dried (also treated with Norit) extract was evaporated *in vacuo*. This gave a viscous oil. It was dissolved in ether, and evaporation gave a yellow powder ($\epsilon_{243-244}$ 4,700), which was dissolved in acetone, treated with Norit and concentrated with simultaneous addition of water; 60 mg., m.p. 198–208° (cloudy melt), ϵ_{243} 9,900. Three recrystallizations from aqueous acetone gave 20 mg. of impure XIII as indicated by u.v. and elemental analyses; m.p. 214–218°, ϵ_{236} 11,300; ϵ_{243} 12,400; and ϵ_{251} 8,300; $[\alpha]_D^{31}$ +10° (8.2 mg., α_D +0.04°).

Anal. Found: C, 76.39; H, 9.41.

Oxido-22a-Allospirostane-7ξ-ol-3-one-ethylene ketal (XIV). The Δ^7-ketal (IX) (0.2 g.) in chloroform (5.5 ml.) was treated with a stock solution of peroxybenzoic acid in benzene (3.5 ml. ≅ 191 mg. peroxy acid), and the mixture was allowed to stand at room temperature for 11 days. It was added to a saturated potassium carbonate solution; the mixture was shaken, and the organic layer was separated. It was washed with water, dried, and evaporated *in vacuo*. This afforded a white powder which on recrystallization from ether-methanol gave 35 mg. of XIV; m.p. 278–280°; no selective absorption in u.v.; λ_{max}^{Nujol} 3534 cm^{-1} (weak hydroxyl), no carbonyl; $[\alpha]_D^{27}$ −66° (22.8 mg., α_D −0.75°), $[M]_D$ −322.

Anal. Calc'd for $C_{29}H_{44}O_6$ (488.64): C, 71.28; H, 9.08.

Found: C, 71.37; H, 9.20.

In another run with IX (2 g.), peroxybenzoic acid in benzene (35 ml. ≅ 1.91 g.), and, chloroform (55 ml.), the mixture was allowed to stand for 13 days at room temperature. There were obtained the following fractions of XIV from ether-methanol; 0.7 g., m.p. 276–277°; 60 mg., m.p. 274–275°, and 210 mg., m.p. 271–274°.

Treatment of XIV with acetic anhydride and pyridine at room temperature gave a product which was partially purified, m.p. 205–209° (from ether-methanol), λ_{max}^{Nujol} no hydroxyl, 1730 cm^{-1} (acetate carbonyl), 1238 cm^{-1} (acetate 'C—O' stretch).

Compound XIV was recovered unchanged, as shown by m.p. and infrared spectrum, from treatment with either lithium aluminum hydride in boiling ether-tetrahydrofuran for two hours or boiling 1% alcoholic potassium hydroxide for one hour.

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SUMMARY

Δ^4-22a-Spirostene-3-one (I) on treatment with ethylene glycol was converted into Δ^5-22a-spirostene-3-one-ethylene ketal (IIa). Hydrolysis gave back the Δ^4-3-one (I). Bromination of IIa with NBS followed by dehydrobromination afforded a 52% yield of pure $\Delta^{5,7}$-22a-spirostadiene-3-one-ethylene ketal (III). $\Delta^{4,7}$-22a-Spirostadiene-3-one (V) was obtained on hydrolysis of the $\Delta^{5,7}$-ketal (III). The latter was also prepared from the $\Delta^{4,7}$-3-one (V).

Both $\Delta^{4,6}$- and $\Delta^{4,7}$-22a-spirostadiene-3-one (IV, V) on acetylation yielded the same enol acetate, $\Delta^{3,5,7}$-22a-spirostatriene-3-ol-acetate (VIII).

Δ^7-22a-Spirostene-3-one-ethylene ketal (IX) was obtained by hydrogenation of the $\Delta^{5,7}$-ketal (III) with a Raney nickel catalyst. Dehydrogenation gave $\Delta^{7,9(11)}$-22a-spirostadiene-3-one-ethylene ketal (X). Hydrolysis afforded $\Delta^{7,9(11)}$-22a-spirostadiene-3-one (XIII). Impure XIII was obtained by dehydrogenation of Δ^7-22a-spirostene-3-one (XII), in turn prepared by hydrolysis of the Δ^7-ketal (IX). Hydroxylation of the Δ^7-ketal (IX) with osmium tetroxide gave 22a-allospirostane-7ξ,8ξ-diol-3-one-ethylene ketal (XI), whereas peroxidation with

peroxybenzoic acid gave oxido-22a-allospirostane-7ξ-ol-3-one-ethylene ketal (XIV).

Another instance of the "abnormal" behavior of ketals in optical rotation analyses has been demonstrated.

A generalization concerning the ultraviolet absorption maxima of $\Delta^{4,7}$-3-ketosteroids has been discussed.

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