Substituent effects in the catalytic hydrogenation of steroidal Δ^4- and Δ^5-3,3-ethyleneketals

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A number of isomeric Δ^4- and Δ^5-3,3-ethylenedioxy steroids were prepared to study the substituent effects on the relative amounts of 5α and 5β ketals formed during catalytic hydrogenation. Hydrogenation of Δ^5-3,3-ethylenedioxy steroids with palladium on charcoal as catalyst yielded 5α steroids exclusively. The Δ^4-3,3-ethylenedioxy compounds yielded mixtures of 5α and 5β ketals in which slightly more 5β product was formed than was obtained by catalytic hydrogenation of the equivalent Δ^4-3-oxo steroid. Substituents in the C-11 position of the Δ^4 ketals diminish the amount of 5β steroid formed during hydrogenation.

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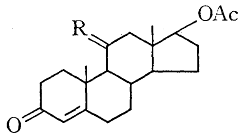
The catalytic hydrogenation of steroidal olefins is known to yield mainly 5β products from Δ^4 compounds and 5α products from the isomeric Δ^5 compounds (1). There have been notable exceptions to the above rule. While studying the catalytic hydrogenation of C-3 substituted cholest-5-enes (2) and cholest-4-enes (3), Shoppee found that the 3β substituents favored the formation of 5α steroids, whereas the 3α substituents promoted β-face hydrogenation, yielding predominantly 5β products. A similar substituent effect was discovered during the catalytic hydrogenation of C-11 oxygenated Δ^4-3-ketones, where the 5α compound was the major product (4).

The foregoing considerations prompted us to investigate the catalytic hydrogenation of Δ^4- and Δ^5-cycloethylenedioxy compounds to assess these effects when they are in juxtaposition, as in the ketals, which have essentially both a 3α and a 3β substituent. The effect of a C-11 ketone and a C-11 β-hydroxyl group on the course of the hydrogenation of ketals was also investigated to determine whether the effects noted in the hydrogenation of Δ^4-3-ketones (4) are duplicated in the hydrogenation of Δ^4 and Δ^5 ketals.

The Δ^4- and Δ^5-3,3-ethylenedioxy ketals of 17β-acetoxyandrost-4-en-3-one (I*a*) (5), 17β-acetoxy-11β-hydroxyandrost-4-en-3-one (I*b*), and 17β-acetoxyandrost-4-en-3,11-dione (I*c*) were prepared by distillation of an ethylene glycol solution of the steroid (6) containing a suitable acid catalyst, either adipic acid or *p*-toluenesulfonic acid (7). The ketalization reactions were monitored by gas–liquid partition chromatography (g.l.p.c.) and the reactions quenched by pouring the mixtures into dilute sodium bicarbonate solutions. The preparation of pure 17β-acetoxy-3,3-ethylenedioxyandrost-4-en-11β-ol (II*b*) by the above method was not practical, since the rate of isomerization of Δ^4 to Δ^5 ketal was comparable to the rate of formation of Δ^4 ketal from the starting ketone I*b*. The product was a mixture of isomeric ketals II*b* and III*b* which could not be separated by crystallization from the usual solvents. Similarly, column chromatography over alumina or Florisil failed to yield pure Δ^4 ketal II*b*. The compound was prepared by sodium borohydride reduction of 17β-acetoxy-3,3-ethylenedioxyandrost-4-en-11-one (II*c*).

The structures of the isomeric ketals were confirmed by nuclear magnetic resonance spectroscopy; the results are given in Table I. The vinylic proton region of the spectra is characteristic; the Δ^4 ketals II*a*, II*b*, and II*c* show a one-proton singlet of width at half-height ($W_{h/2}$) $\simeq 3.5$ c.p.s., whereas the Δ^5 ketals III*a*, III*b*, and III*c* exhibit a broad multiplet of $W_{h/2} \simeq 8.7$ c.p.s. The positions of the C-19 proton resonances were in agreement with those calculated from the additivity values (8) for the Δ^5-3,3-ethylenedioxy ketals. Examination of the spectra of the Δ^4 ketals II*a*, II*b*, and II*c* suggests that the 3,3-ethylenedioxy group in Δ^4 steroids has no influence on the chemical shift of the C-19 and C-18 protons (Table I).



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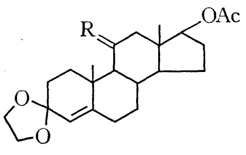

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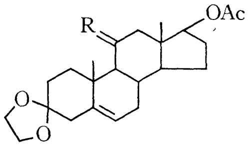

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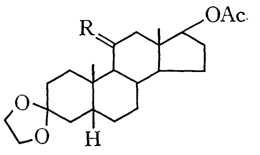

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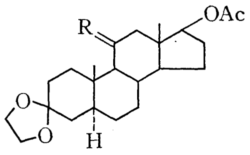

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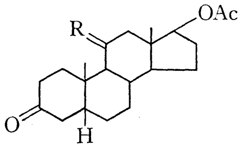

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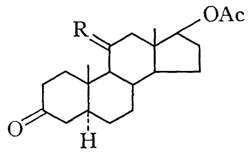

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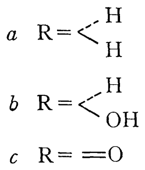

TABLE I

Nuclear magnetic resonance spectra of Δ^4 and Δ^5 ketals

Compound	Vinylic proton		Experimental δ (p.p.m.)		Calculated δ (p.p.m.)	
	δ (p.p.m.)	$W_{h/2}$ (c.p.s.)	C-19 protons	C-18 protons	C-19 protons	C-18 protons
II*a*	5.18	3.3	1.04	0.82	1.042	0.817
III*a*	5.44	9.0	1.05	0.81	1.050	0.834
II*b*	5.11	3.7	1.31	1.06	1.300	1.059
III*b*	5.28	8.5	1.31	1.05	1.308	1.076
II*c*	5.25	3.5	1.25	0.74	1.259	0.784
III*c*	5.29	9.0	1.24	0.78	1.267	0.801

The hydrogenations were carried out with palladium on charcoal as catalyst because of the ease with which the reaction can be carried out and also because the yields of 3-oxo-5β steroids are generally highest with this catalyst (9). Solvent effects have been noted in palladium-catalyzed hydrogenations of Δ^4-3-ketones, the more polar hydroxylic solvents favoring the formation of 5β steroids (10). The hydrogenations were all performed under identical conditions and the crude products were analyzed by g.l.p.c. In Table II are listed the ratios of 5α and 5β ketals obtained, neglecting the hydrogenolysis side products which are found in the catalytic hydrogenation of the Δ^4 ketals II*a*, II*b*, and II*c*. Analysis by g.l.p.c. indicated that up to 40% of unidentified hydrogenolysis products were formed in the catalytic hydrogenation of II*c*. Quantitation of the mixture of C-5 isomers generated in the catalytic hydrogenation of 17β-acetoxy-3,3-ethylenedioxyandrost-4-en-11β-ol (II*b*) and 17β-acetoxy-3,3-ethylenedioxyandrost-4-

TABLE II

Ratios of 5α and 5β steroids formed during the catalytic hydrogenation of Δ^4 and Δ^5 ketals

Compound	5β ketal	5α ketal
II*a*	72% IV*a*	28% V*a*
II*b*	17% IV*b*	83% V*b*
II*c*	38% IV*c*	62% V*c*
III*a*	0% IV*a*	100% V*a*
III*b*	0% IV*b*	100% V*b*
III*c*	0% IV*c*	100% V*c*

TABLE III

Nuclear magnetic resonance spectra of 5α- and 5β-3,3-ethylenedioxy ketals

	Experimental δ (p.p.m.)		Calculated δ (p.p.m.)		$W_{h/2}$ (c.p.s.)		
Compound	C-19 protons	C-18 protons	C-19 protons	C-18 protons	C-19 protons	Tetramethylsilane	$\Delta W_{h/2}$ (c.p.s.)
IV*a*	0.96	0.78	0.958	0.775	0.95	0.38	0.57
V*a*	0.82	0.79	0.825	0.775	1.60	0.58	1.02
IV*b*	1.20	1.02	1.216	1.017	1.06	0.56	0.50
V*b*	1.07	1.02	1.083	1.017	1.60	0.58	1.02
IV*c*	1.18	0.74	1.175	0.742	1.08	0.64	0.44
V*c*	1.04	0.73	1.042	0.742	1.40	0.58	0.82

en-11-one (II*c*) was not possible because the mixtures were not completely resolved by g.l.p.c. Mild hydrolysis with acetic acid (11) to convert the ketals into mixtures of 3-oxo-5α (VI*b* and VI*c*) and 3-oxo-5β steroids (VII*b* and VII*c*) was employed; g.l.p.c. analysis was used to determine the ratios of 3-oxo-5α and 3-oxo-5β steroids (Table II).

The 5α ketals V*a*, V*b*, and V*c* were all identified by characterizing the products of the catalytic hydrogenation of the Δ^5 ketals III*a*, III*b*, and III*c*, respectively. The 5β ketals IV*a*, IV*b*, and IV*c* were prepared from authentic 3-oxo-5β-steroids VI*a*, VI*b*, and VI*c*. The nuclear magnetic resonance spectra of the isomeric ketals are recorded in Table III, and the chemical shifts of the C-19 and C-18 protons are compared with those calculated from the additivity values for steroid methyl protons (8). The stereochemical assignments were further confirmed by using the method of Williamson *et al.* (12) for measuring the line widths of the angular methyl groups. The $W_{h/2}$ of the C-19 methyl group less that of the tetramethylsilane signal gives a $\Delta W_{h/2}$ which is larger for 5α steroids than for the corresponding 5β steroids.

Catalytic hydrogenation of the Δ^5 ketals III*a*, III*b*, and III*c* gave excellent yields of 5α steroids V*a*, V*b*, and V*c* uncontaminated by the corresponding 5β isomers. The hydrogenation of Δ^5-3,3-ethylenedioxy ketals in neutral media is of preparative value and can be considered as an alternate method to metal–ammonia reduction for the preparation of 3-oxo-5α steroids from Δ^4-3-oxo compounds.

A comparison of the hydrogenation results obtained with 17β-acetoxyandrost-4-en-3-one (I*a*) (Table IV) and 17β-acetoxy-3,3-ethylenedioxyandrost-4-ene (II*a*) (Table II) indicates a 16% greater yield of 5β product formed as a result of the introduction of the ketal. This effect is probably due to increased shielding of the α face of the steroid. As the β face of the steroid becomes more hindered by C-11 substituents, this effect diminishes. With the C-11 oxo compounds I*c* and II*c*, the preponderance of 5β product from II*c* is only 9%, whereas the C-11 hydroxy steroids I*b* and II*b* do not demonstrate this preferential β-face hydrogenation.

TABLE IV

Ratios of 5α and 5β steroids formed during the catalytic hydrogenation of Δ^4-3-oxo steroids

Compound	5β product	5α product
I*a*	56% VI*a*	44% VII*a*
I*b*	37% VI*b*	63% VII*b*
I*c*	29% VI*c*	71% VII*c*

EXPERIMENTAL

General

Melting points were determined on an Electrothermal apparatus by the capillary method and are corrected. Rotations were measured in chloroform solution. Infrared spectra were recorded on a Perkin–Elmer model 237B double-beam spectrophotometer. Gas–liquid partition chromatography was carried out on a model 810 F and M gas chromatograph equipped with dual-flame detectors. The columns (8 ft × 4 mm outside diameter) contained 5% fluoro silicone FS-1265 (QF-1) on 60–80 mesh Diatoport "S". The carrier gas was helium at a flow rate of 60 ml/min. Unless specified otherwise, the column temperature was 230°. Quantitative estimation of the mixtures was made by triangulation of the signals.

Nuclear magnetic resonance spectra were determined on a Varian A-60A spectrometer equipped with a Varian C-1024 time-averaging computer (CAT) in deuteriochloroform containing 1% tetramethylsilane as an internal standard. The carbon and hydrogen microanalyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, New York.

17β-Acetoxy-3,3-ethylenedioxyandrost-4-ene (IIa)

A solution of testosterone acetate (I*a*) (3 g) in ethylene glycol (125 ml) containing adipic acid (560 mg) was distilled slowly (5 h) at 70–90° and 0.1 mm until approximately half of the glycol was distilled. The solution was chilled and the product crystallized. The product was removed by filtration and washed with sodium bicarbonate solution (100 ml) and then with water containing 1% pyridine. The ketal (3.3 g) was dried *in vacuo* and recrystallized from hexane – 1% pyridine. The 17β-acetoxy-3,3-ethylenedioxyandrost-4-ene (II*a*) (1.5 g) (m.p. 157–158°) was analyzed by g.l.p.c.; two compounds having retention times of 9.0 (Δ^4 ketal, 92%) and 10.0 min (Δ^5 ketal III*a*, 8%) were detected. Recrystallization from hexane – 1% pyridine gave a homogeneous compound, retention time 9.0 min (210°), m.p. 158–159°, $[\alpha]_D^{26}$ + 75.1° (*c*, 1.0) (lit. (5) m.p. 159–161°, $[\alpha]_D^{25}$ + 80°); infrared: ν_{max}^{Nujol} 1 728 ($-OCOCH_3$), 1 660 (C=C), and 1 090 and 1 040 cm^{-1} (ketal).

17β-Acetoxy-3,3-ethylenedioxyandrost-5-ene (IIIa)

A solution of testosterone acetate (I*a*) (1.5 g) in ethylene glycol (150 ml) containing *p*-toluenesulfonic acid (120 mg) was distilled as described above. The reaction mixture was poured into water (1 l) containing pyridine (15 ml) and stirred for 30 min. The solid material was removed by filtration, washed with water, and air dried (995 mg). The 17β-acetoxy-3,3-ethylenedioxyandrost-5-ene (III*a*) was crystallized from acetone–hexane (568 mg), m.p. 198–200°, $[\alpha]_D^{25}$ – 51.8° (*c*, 0.9) (lit. (5) m.p. 203–205°, $[\alpha]_D^{29}$ – 52.1°); analysis by g.l.p.c. (210°) demonstrated a single peak with a retention time of 10.0 min; infrared: $\nu_{max}^{CCl_4}$ 1 732 ($-OCOCH_3$), 1 095, and 1 030 cm^{-1} (ketal).

17β-Acetoxy-3,3-ethylenedioxyandrost-4-en-11-one (IIc)

A solution of 17β-acetoxyandrost-4-en-3,11-dione (I*c*), m.p. 159–161° (lit. (13) m.p. 162–163°) (2 g) in ethylene glycol (125 ml) containing adipic acid (350 mg) was treated as described in the preparation of II*a*. Analysis of the crude reaction product (1.9 g) by g.l.p.c. gave peaks with retention times of 11.5 and 13 min, representing 23% 17β-acetoxy-3,3-ethylenedioxyandrost-5-en-11-one (III*c*) and 77% 17β-acetoxy-3,3-ethylenedioxyandrost-4-en-11-one (II*c*), respectively. The material was chromatographed over Florisil (60 g) and the column was eluted with anhydrous benzene. The more mobile 17β-acetoxy-3,3-ethylenedioxyandrost-4-en-11-one (II*c*) (800 mg) was recrystallized from hexane – 1% pyridine, m.p. 141°, $[\alpha]_D^{27}$ + 105° (*c*, 1.1); infrared: $\nu_{max}^{CCl_4}$ 1 739 ($-OCOCH_3$), 1 708 (C=O), 1 661 (C=C), and 1 090, 1 047, and 1 025 cm^{-1} (ketal). Analysis by g.l.p.c. indicated that the compound was homogeneous (peak with a retention time of 13 min).

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.33; H, 8.30.

17β-Acetoxy-3,3-ethylenedioxyandrost-5-en-11-one (IIIc)

Further elution of the above column yielded 17β-acetoxy-3,3-ethylenedioxyandrost-5-en-11-one (III*c*) (360 mg). Recrystallization from hexane – 1% pyridine gave pure III*c* (260 mg), m.p. 170–173°, $[\alpha]_D^{26}$ – 118° (*c*, 1.2); infrared: $\nu_{max}^{CCl_4}$ 1 741 ($-OCOCH_3$), 1 706 (C=O), and 1 094, 1 047, and 1 032 cm^{-1} (ketal); g.l.p.c. gave a single peak with a retention time of 11.5 min.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.38; H, 8.52.

17β-Acetoxy-3,3-ethylenedioxyandrost-4-en-11β-ol (IIb)

A solution of 17β-acetoxy-3,3-ethylenedioxyandrost-4-en-11-one (II*c*) (132 mg) in absolute ethanol (15 ml) was treated with sodium borohydride (130 mg) for 18 h at room temperature. The solvent was evaporated under reduced pressure and the residue was dissolved in dichloromethane (50 ml) and water (50 ml). The organic layer was washed with salt solution, dried over sodium sulfate, filtered, and evaporated under vacuum. The 17β-acetoxy-3,3-ethylenedioxyandrost-4-en-11β-ol (II*b*) was crystallized from acetone–hexane (110 mg), m.p. 169–170.5°, $[\alpha]_D^{26}$ + 115° (*c*, 0.9); infrared: $\nu_{max}^{CCl_4}$ 1 738 ($-OCOCH_3$), 1 659 (C=C), and 1 090, 1 040, and 1 025 cm^{-1} (ketal). Analysis by g.l.p.c. indicated that the compound was homogeneous (peak with a retention time of 9.6 min).

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.73; H, 8.77. Found: C, 70.33; H, 8.95.

17β-Acetoxy-3,3-ethylenedioxyandrost-5-en-11β-ol (IIIb)

A solution of 17β-acetoxy-11β-hydroxyandrost-4-en-3-one (I*b*) (1.0 g, m.p. 151°) (lit. (14) m.p. 149.5–151.5°) in ethylene glycol (125 ml) was treated as in the preparation of III*a*. The product III*b* (950 mg, m.p. 183.5–185.5°) was identical with the authentic material previously prepared (15).

Catalytic Hydrogenation of 17β-Acetoxy-3,3-ethylenedioxyandrost-4-ene (IIa)

A mixture of II*a* (800 mg) and 10% palladium on charcoal (400 mg) in absolute ethanol (100 ml) was hydrogenated at room temperature and atmospheric pressure until the uptake of hydrogen ceased (2.5 h). The solution was filtered through Celite and evaporated to dryness. Analysis of the crude product by g.l.p.c. (213°) gave peaks with retention times of 11.2 and 12.2 min, representing 72% 17β-acetoxy-3,3-ethylenedioxy-5β-androstane (IV*a*) and 28% 17β-acetoxy-3,3-ethylenedioxy-5α-androstane (V*a*), respectively.

The mixture of IV*a* and V*a* (500 mg) was separated by column chromatography over Florisil (40 g). The 17β-acetoxy-3,3-ethylenedioxy-5β-androstane (IV*a*) (104 mg) was eluted with 4:1 hexane–benzene and recrystallized from ethanol – 1% pyridine, m.p. 120.5–121.5° (lit. (16) m.p. 120°), $[\alpha]_D^{26} + 19.9°$ (c, 1.0); infrared: $\nu_{max}^{CCl_4}$ 1 735 and 1 248 (—$OCOCH_3$), 1 090, and 1 025 cm^{-1} (ketal). Analysis by g.l.p.c. gave a peak with a retention time of 11.2 min.

Ketal IV*a* (20 mg) was dissolved in 75% acetic acid (1.5 ml) and heated on a steam bath (30 min). The solution was diluted with ether (10 ml), washed with sodium bicarbonate solution (3 × 20 ml) and then with salt solution, dried over sodium sulfate, filtered, and evaporated to dryness. The residual oil (17 mg) was crystallized from acetone–hexane, m.p. 140–142°; a mixture melting point with the authentic 17β-acetoxy-5β-androstan-3-one (VI*a*) previously prepared (17) showed no depression.

Catalytic Hydrogenation of 17β-Acetoxy-3,3-ethylenedioxyandrost-5-ene (IIIa)

A solution of the Δ^5 ketal III*a* (475 mg) in ethanol (60 ml) was hydrogenated over 10% palladium on charcoal (225 mg) at atmospheric pressure. After the absorption of 1 molar equivalent of hydrogen (1.5 h), the product was isolated in the usual manner. Analysis of the crude product by g.l.p.c. revealed the presence of a single peak with a retention time of 12.2 min. The 17β-acetoxy-3,3-ethylenedioxy-5α-androstane (V*a*) was crystallized from ethanol – 1% pyridine (114 mg), m.p. 138°, $[\alpha]_D^{25} + 11°$ (c, 1.0) (lit. (18) m.p. 139–140°, $[\alpha]_D + 3°$); infrared: $\nu_{max}^{CCl_4}$ 1 731 and 1 235 (—$OCOCH_3$), 1 095 and 1 022 cm^{-1} (ketal).

Ketal V*a* (20 mg) was hydrolyzed as in the previous experiment and the product crystallized from acetone–hexane, m.p. 158–160°; a mixture melting point with authentic 17β-acetoxy-5α-androstan-3-one (VII*a*) was undepressed.

Catalytic Hydrogenation of 17β-Acetoxy-3,3-ethylenedioxyandrost-4-en-11β-ol (IIb)

A solution of the Δ^4 ketal II*b* (90 mg) in ethanol (10 ml) was hydrogenated (3 h) over 10% palladium on charcoal (42 mg) as previously described, and the crude product was isolated in the usual manner. Analysis by g.l.p.c. gave a partly resolved peak with a retention time of 9.8 min, which consisted of a mixture of IV*b* and V*b*. Mixtures of authentic IV*b* and V*b* prepared below also gave a similar peak with a retention time of 9.8 min. The crude material (75 mg) was treated with 75% acetic acid (5 ml) as previously described and the hydrolysate isolated in the usual fashion. Analysis by g.l.p.c. gave peaks at 18.1 and 20.0 min, which corresponded to 17% 17β-acetoxy-11β-hydroxy-5β-androstan-3-one (VI*b*) and 83% 17β-acetoxy-11β-hydroxy-5α-androstan-3-one (VII*b*), respectively. The compounds were identified by peak enhancement with authentic VI*b* and VII*b*.

Catalytic Hydrogenation of 17β-Acetoxy-3,3-ethylenedioxyandrost-5-en-11β-ol (IIIb)

Catalytic hydrogenation of III*b* (300 mg) was carried out as previously described and the crude product was shown to be homogeneous by g.l.p.c. After evaporation of the solvent, the product crystallized (287 mg), m.p. 192–193°. Recrystallization from acetone–hexane gave pure 17β-acetoxy-3,3-ethylenedioxy-5α-androstan-11β-ol (V*b*) (260 mg), m.p. 192–193°, $[\alpha]_D^{28} + 11°$ (c, 1.0); infrared: $\nu_{max}^{CCl_4}$ 1 738 and 1 242 (—$OCOCH_3$), 1 090, and 1 025 cm^{-1} (ketal). Analysis by g.l.p.c. revealed a single peak with a retention time of 9.8 min.

Anal. Calcd. for $C_{23}H_{36}O_5$: C, 70.4; H, 9.24. Found: C, 70.3; H, 9.4.

An aliquot of ketal V*b* (20 mg) was hydrolyzed with acetic acid as previously described and the hydrolysate was analyzed by g.l.p.c. A single peak with a retention time of 20.0 min was detected; the latter was enhanced by authentic 17β-acetoxy-11β-hydroxy-5α-androstan-3-one (VII*b*) (15).

17β-Acetoxy-3,3-ethylenedioxy-5β-androstan-11β-ol (IVb)

A solution of 17β-acetoxy-11β-hydroxy-5β-androstan-3-one (VI*b*) (61 mg, m.p. 126.5–127°) (15) in ethylene glycol (50 ml) containing *p*-toluenesulfonic acid (10 mg) was subjected to the usual ketal-forming conditions. Analysis of the crude product by g.l.p.c. gave a single peak with a retention time of 9.8 min. The 17β-acetoxy-3,3-ethylenedioxy-5β-androstan-11β-ol (59 mg) was chromatographed over Florisil (12 g) and eluted with benzene. Ketal IV*b* (50 mg) was crystallized from acetone–hexane, m.p. 119–120°, $[\alpha]_D^{26} - 12°$ (c, 0.9); infrared: $\nu_{max}^{CCl_4}$ 3 630 (OH), 1 740 and 1 246 (—$OCOCH_3$), 1 090, and 1 029 cm^{-1} (ketal).

Anal. Calcd. for $C_{23}H_{36}O_5$: C, 70.4; H, 9.24. Found: C, 70.58; H, 9.43.

Catalytic Hydrogenation of 17β-Acetoxy-3,3-ethylenedioxyandrost-5-en-11-one (IIIc)

A solution of III*c* (170 mg) in ethanol (15 ml) was hydrogenated (3 h) over palladium on charcoal (80 mg) as previously described. The reaction mixture was filtered free of catalyst and the solvent was removed, leaving an oil (165 mg), which was shown to be homogeneous by g.l.p.c. (peak with a retention time of 11.2 min). The product, 17β-acetoxy-3,3-ethylenedioxy-5α-androstan-11-one (V*c*), crystallized from hexane (148 mg), m.p. 169–170°, $[\alpha]_D^{26} - 85°$ (c, 1.0); infrared: $\nu_{max}^{CCl_4}$ 1 739 and 1 238 (—$OCOCH_3$), 1 708 (C=O), 1 098, and 1 030 cm^{-1} (ketal).

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.73; H, 8.77. Found: C, 70.81; H, 8.69.

Ketal V*c* (120 mg) was hydrolyzed with 75% acetic acid (5 ml) as previously described. After removal of the solvent, the crude material (102 mg) was crystallized from ethanol to give 17β-acetoxy-5α-androstan-3,11-dione (VII*c*), m.p. 147–148°, $[\alpha]_D^{25} - 20°$ (c, 1.1); infrared: $\nu_{max}^{CCl_4}$ 1 743 and 1 239 (—$OCOCH_3$) and 1 713 cm^{-1} (C=O). Analysis by g.l.p.c. gave a single peak with a retention time of 14.8 min.

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 73.07; H, 8.89.

Catalytic Hydrogenation of 17β-Acetoxy-3,3-ethylenedioxyandrost-4-en-11-one (IIc)

A solution of II*c* (10 mg) in ethanol (3 ml) was hydrogenated (3 h) over palladium on charcoal (5 mg) as described above. The reaction mixture was filtered and the solvent evaporated. Analysis of the crude product by g.l.p.c. gave a broad, partly resolved peak with a retention time of 11.4 min. Mixtures of authentic 5α ketal V*c* and 5β ketal IV*c* gave similar g.l.p.c. results.

The product, an unresolved mixture of 17β-acetoxy-3,3-ethylenedioxy-5α-androstan-11-one (V*c*) and 17β-acetoxy-3,3-ethylenedioxy-5β-androstan-11-one (IV*c*), was hydrolyzed with 75% acetic acid as previously described. After removal of the solvent, the crude oil (7 mg) was analyzed by g.l.p.c.; two peaks were detected with retention times of 13.6 and 15.4 min, representing 39% 17β-acetoxy-5β-androstan-3,11-dione (VI*c*) and 61% 17β-acetoxy-5α-androstan-3,11-dione (VII*c*). The compounds were identified by peak enhancement with the 5α ketone VII*c* previously prepared and with the authentic 5β ketone VI*c* prepared below.

17β-Acetoxy-5β-androstan-3,11-dione (VIc)

A solution of 17β-acetoxy-11β-hydroxy-5β-androstan-3-one (VI*b*) (120 mg) in pyridine (1.2 ml) was added to a stirred suspension of chromium trioxide (115 mg) in pyridine (1.1 ml). The suspension was stirred at room temperature (1.2 h) and the reaction quenched by the addition of ether (50 ml) and sodium bicarbonate solution (50 ml). The organic layer was washed with sodium bicarbonate solution until colorless, and then with 3 *N* hydrochloric acid (100 ml) and sodium chloride solution until neutral. The ether solution was dried over sodium sulfate, filtered, and evaporated under reduced pressure. The residue was crystallized from acetone–hexane to give pure 17β-acetoxy-5β-androstan-3,11-dione (VI*c*) (102 mg), m.p. 194–194.5°, $[\alpha]_D^{25} + 39°$ (*c*, 0.7); infrared: $\nu_{\max}^{\mathrm{CCl_4}}$ 1 738 and 1 235 ($-OCOCH_3$) and 1 712 cm^{-1} ($C{=}O$). Analysis by g.l.p.c. gave a single peak with a retention time of 13.6 min.

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.83. Found: C, 72.90; H, 8.88.

17β-Acetoxy-3,3-ethylenedioxy-5β-androstan-11-one (IVc)

A solution of 17β-acetoxy-5β-androstan-3,11-dione (VI*c*) in ethylene glycol (50 ml) containing *p*-toluenesulfonic acid (11 mg) was treated as previously described and the 17β-acetoxy-3,3-ethylenedioxy-5β-androstan-11-one (IV*c*) was isolated in the usual manner. The crude product (56 mg) was crystallized from hexane (28 mg), m.p. 154–155°, $[\alpha]_D^{25} + 33.8°$ (*c*, 0.7); infrared: $\nu_{\max}^{\mathrm{CCl_4}}$ 1 739 ($-OCOCH_3$), 1 709 ($C{=}O$), 1 090, and 1 020 cm^{-1} (ketal). Analysis by g.l.p.c. gave a single peak with a retention time of 19.2 min.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.73; H, 8.77. Found: C, 70.56; H, 8.76.

Catalytic Hydrogenation of Δ^4-3-Oxo-Steroids Ia, Ib, and Ic

The catalytic hydrogenation of 17β-acetoxyandrost-4-en-3-one (I*a*), 17β-acetoxy-11β-hydroxyandrost-4-en-3-one (I*b*), and 17β-acetoxyandrost-4-en-3,11-dione (I*c*) was carried out by dissolving the steroid (10 mg) in ethanol (1.1 ml) containing 10% palladium on charcoal (5 mg) and stirring at room temperature for 45 min. The reaction mixture was filtered through Celite and evaporated to dryness. The crude products were analyzed by g.l.p.c. and the peaks were identified by peak enhancement with authentic 5α steroids VII*a*, VII*b*, and VII*c* and 5β steroids VI*a*, VI*b*, and VI*c*. The results are listed in Table IV.

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