$$r = \frac{K_1K_2k_5[D][Rh]_{total}}{[P] + K_1} \quad (4)$$

From eq 4, eq 5 is derived.

$$1/r = \frac{1}{K_2k_5[D][Rh]_{total}} + \frac{[P]}{K_1K_2k_5[D][Rh]_{total}} \quad (5)$$

The linear relationship between the reciprocal of the rate and the concentration of phosphine was also satisfied by the experiment shown in Figure 5.

By assuming that the concentrations of olefin, the alcohol, the catalyst, and phosphine may be regarded as almost constant at the initial stage of the transfer hydrogenation, eq 6 is derived from eq 1, where α and β are constants, and the assumption seems to be not so unreasonable. The linearity between the reciprocal of the rate and the concentration of acetone is shown in Figure 5.

$$1/r = \alpha[\text{acetone}] + \beta \quad (6)$$

As described above, eq 1 or 4 is not contradictory to any observed fact and is able to explain all the experimental results. This supports the proposed reaction scheme.

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Catalytic Hydrogenolysis of Lumitestosterone Acetate

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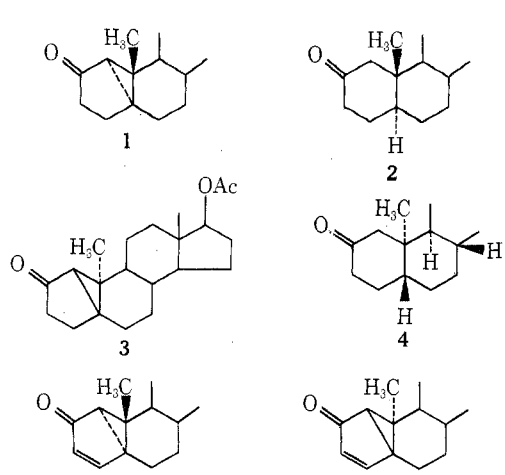
The hydrogenolysis of lumitestosterone acetate (**3**) over palladium in ethanol gave a mixture of products from which 17β-acetoxy-5α,10α-androstane (**7**), 5α-ethoxy-17β-acetoxy-10α-androstane (**9a**), and 17β-acetoxy,5α,10α-androstan-2α-ol (**12**) were isolated. These same products were also obtained from the Raney nickel catalyzed hydrogenolysis of **3**. In the later reaction a very small amount of 17β-acetoxy-5β,10α-androstan-2α-ol (**18**) was also obtained. The lack of stereoselectivity in this hydrogenolysis led to the proposal of a mechanistic rationale involving an initial catalytic isomerization of **3** to 17β-acetoxy-10α-androst-5-en-2-one (**17**) followed by the hydrogenation of **17** to give the 5α products.

While it appears that alkyl-substituted cyclopropane hydrogenolysis is nonstereoselective,[2] some reports have indicated that the hydrogenolysis of cyclopropyl ketones[3,4] or esters[5] is a stereoselective process. For instance, it has been shown[4] that the hydrogenolysis of a 10β-methyl-1α,5α-cyclo-2-keto steroid, **1**, gives only the 5α product, **2**, by what appears to be a stereospecific cleavage of the 1α,5α bond of the cyclopropane ring. In light of these reports it was felt that the hydrogenolysis of a 10α-methyl-1β,5β-cyclo-2-keto steroid such as lumitestosterone acetate (**3**) should provide a reasonable access route to the rather difficultly available 10α,5β steroids, **4**. This assumption was further supported by an examination of a molecular model of **3** which showed that the 1,5 bond was the most readily accessible to the catalyst surface of the three cyclopropane bonds in **3**.

It should be noted, though, that the ring cleavage in the 10α-methyl compounds (*e.g.*, **3**) is not as facile as it is in the 10β-methyl series (**1**). Hydrogenation of the Δ^3-10β-methyl-1α,5α-cyclo steroid, **5**, over palladium at room temperature and atmospheric pressure gave a 2:1 mixture of compounds **1** and **2**.[4a] Under comparable conditions hydrogenation of the Δ^3-10α-methyl-1β,5β-cyclo steroids, **6**, gave only the cyclopropyl ketones, such as **3**, with no ring-opened material formed.[6]



Experimental Section

Melting points are uncorrected and were measured in open capillary tubes using a Mel-Temp apparatus. The infrared spectra were obtained using a Beckman IR-10 spectrophotometer and the pmr spectra were recorded with a Varian A-60A spectrometer using deuteriochloroform as the solvent with TMS as an internal standard. Atmospheric pressure hydrogenations were carried out in a sloping manifold apparatus[7] while the high-pressure hydrogenations were run in a 300-ml Autoclave Engineers Magnedrive Autoclave.

Woelm neutral alumina was used for the column chromatographies and the thin layer chromatographies (tlc) were run using microscope slides immersed in a chloroform suspension of Woelm tlc-grade neutral alumina with iodine as the visualization reagent. Gas chromatographic (glpc) analyses were run using a Varian Aerograph Model 204-1B flame ionization chromatograph with a 6 ft × 0.25 in. column containing 1% QF-1 on 100–120 mesh Aeropak 30 at 280°, unless otherwise specified. Elemental analyses were performed by Micro-Analysis, Inc., Wilmington, Del.

Lumitestosterone acetate (3) was prepared using the procedure described by Chapman:[8] mp 166–167° (lit.[8] mp 167–169°); nmr δ 0.78 (s, 3, 18-CH_3), 1.17 (s, 3, 19-CH_3), 1.65 (s, 1, 1-H), 2.03 (s, 3, 17-Ac) and 4.62 (t, 1, J = 7.5 Hz, 17α-H).

Hydrogenolysis of 3 over Palladium. A mixture of 156 mg of **3**, 75 mg of 5% palladium on charcoal, and 50 ml of absolute ethanol was stirred under 1600 psig of hydrogen for 22 hr at 120–130°. After cooling, the catalyst was removed by filtration through Celite and the solvent was evaporated. The residue was chromatographed on alumina (97 × 13 mm, activity III) and the composition of the fractions was monitored by glpc analysis. Elution with 2% benzene in hexane gave three fractions. Fraction A (51 mg) contained three compounds in a 1:2.5:14 ratio. Recrystallization from methanol gave a pure sample of the major component, 17β-acetoxy-5α,10α-androstane (**7**): mp 103.5–104°; ir ($CHCl_3$) 2930, 2860, 1725, 1450, 1375, 1260, and 1040 cm^{-1}; nmr δ 0.78 (s, 3, 18-CH_3), 1.02 (s, 3, 19-CH_3), 2.03 (s, 3, 17-Ac), and 4.62 (t, 1, J = 7.5 Hz, 17α-H). **7** was dissolved in a mixture of 4 ml of methanol and 0.5 ml of 10% aqueous sodium hydroxide and the resulting solution was stirred at room temperature for 18 hr. After neutralization and extraction a solid was obtained which on recrystallization from hexane gave 5α,10α-androstan-17β-ol (**8**), mp 155–157° (lit.[9] mp 159°).

Fraction B, 9 mg of an oil, was homogeneous by glpc analysis. The spectral and chromatographic data on this material showed it to be identical with the ethoxy compound, **9a**, which was also formed by the Raney nickel hydrogenolysis of **3** (*vide infra*).

Fraction C, 13 mg of an oil, was also found to be homogeneous by glpc analysis. This material was tentatively assigned structure **11**, nmr δ 0.78 (s, 3, 18-CH_3), 1.04 (d, 3, J = 7 Hz, 19-CH_3), 2.02 (s, 3, 17β-Ac), and 4.62 (t, 1, J = 7.5 Hz, 17α-H).

Fraction D, 94 mg, was eluted with benzene, ir 1725 (acetate), 3440, and 3600 cm^{-1} (OH). This fraction was shown by chromatographic and spectral comparisons to be composed of about 80% of 17β-acetoxy-5α,10α-androstan-2α-ol (**12a**), 15% of the 2β epimer (**13a**), and small amounts of other materials. This mixture was hydrolyzed at room temperature with methanolic sodium hydroxide and neutralized, and the isolated product was chromatographed on activity III alumina. Elution with benzene gave a small amount of an oil; with ether 33 mg of a solid was obtained which on recrystallization from acetone–hexane gave 5α,10α-androstane-2α,17β-diol (**12b**), mp 190–193° (lit.[10] mp 192–195°).

The product distributions observed on hydrogenolysis of **3** over palladium on charcoal under other conditions are given in Table I.

Hydrogenolysis of 3 over Raney Nickel. A. Low Temperature. A mixture of 156 mg of **3**, about 0.5 g of W-2 Raney nickel,[11] and 75 ml of absolute ethanol was stirred at 50–60° under 1300 psig of hydrogen for 7 hr. Removal of the catalyst and evaporation of the solvent gave a residue with spectral characteristics nearly identical with those of the mixture of the 2α- and 2β-cyclopropylcarbinols, **14** and **15**, obtained from the hydride reduction of **3** as described below. Reoxidation of the hydrogenation product with CrO_3–pyridine gave an 80% yield of **3**.

B. Higher Temperature. A mixture of 1 g of **3**, ~4 g of W-2 Raney nickel,[11] and 100 ml of absolute ethanol was stirred at 80° under 1300 psig of hydrogen for 24 hr. The catalyst was removed, the solvent was evaporated, and the residue was chromatographed on alumina (220 × 25 mm, activity III) which had been washed with 10% benzene in hexane. The composition of the fractions was monitored by glpc analysis on a QF-1 column at 208°.

Table I
Product Distribution from the Hydrogenolysis of 3 over 5% Palladium on Carbon[a]

Temp, °C	Solvent	Fraction, %[b] A	B	C	D
90–100	EtOH	17	3	8	50
120–130	EtOH	32	5	8	50
140	EtOH	50	7	2	41
140	EtOAc	45			53
110–120	EtOAc	~20% reaction to form **13b**			

[a] 25 mg of catalyst, 100 mg of **3**, 100 ml of solvent, 24 hr, 1500 psig hydrogen. [b] The rest of the material was recovered **3**.

Fraction A, 376 mg, which was eluted with 10% benzene in hexane, was found by chromatographic analysis to be composed of two compounds in a 1:4 ratio. Recrystallization from methanol gave the major component, identified as **7**, mp 95–99°. The minor component was identical with one of the minor 2-deoxy compounds formed during the palladium-catalyzed hydrogenolysis of **3**, but it was not characterized further.

Fraction B, 200 mg, which was also eluted with 10% benzene in hexane, was homogeneous as shown by glpc and tlc analysis. Recrystallization from methanol gave 17β-acetoxy-5α-ethoxy-10α-androstane (**9a**): mp 101.5–103°; ir ($CHCl_3$) 2930, 2870, 1725, 1465, 1445, 1375, 1260, 1110, 1075, 1040, and 1025 cm^{-1}; nmr δ 0.78 (s, 3, 18-CH_3), 0.97 (s, 3, 19-CH_3), 1.09 (t, 3, J = 7 Hz, -OCH_2CH_3), 2.01 (s, 3, 17β-Ac), and 3.26 (q, 2, J = 7 Hz, -OCH_2CH_3). *Anal.* Calcd for $C_{23}H_{38}O_3$: C, 76.20; H, 10.56. Found: C, 76.48; H, 10.67.

Hydrolysis of **9a** with methanolic NaOH gave 5α-ethoxy-10α-androstan-17β-ol (**9b**): mp 191–191.5° from acetone–hexane; ir ($CHCl_3$) 3593, 3450, 2930, 2870, 1465, 1445, 1375, 1110, and 1070 cm^{-1}; nmr δ 0.73 (s, 3, 18-CH_3), 0.99 (s, 3, 19-CH_3), 1.11 (t, 3, J = 7 Hz, -OCH_2CH_3), 3.28 (q, 2, J = 7 Hz, -OCH_2CH_3), and 3.65 (t, 1, J = 8 Hz, 17α-H). *Anal.* Calcd for $C_{21}H_{36}O_2$: C, 78.70; H, 11.32. Found: C, 78.82; H, 11.43.

Fraction C, 425 mg, which was eluted with 10% ether in benzene, was a mixture of compounds as shown by chromatographic and spectral analysis. This fraction was rechromatographed on a 165 × 13 mm column of activity IV alumina. Elution with carbon tetrachloride gave 46 mg of an oil which was shown to be **14** contaminated with **3** and a small amount of a third component. Further elution with carbon tetrachloride gave 290 mg of a solid which was shown by nmr analysis to be predominantly the cyclopropylcarbin-2β-ol **15** contaminated with small amounts of several other species. Elution with chloroform gave 26 mg of an oil which was shown to be nearly homogeneous by chromatographic analysis but which could not be induced to crystallize. This material has been tentatively assigned the structure 17β-acetoxy-5β,10α-androstan-2α-ol (**18**): ir ($CHCl_3$) 3520, 3460, 2930, 2850, 1715, 1450, 1370, 1255, and 1040 cm^{-1}; nmr δ 0.85 (s, 3, 18-CH_3), 1.28 (s, 3, 19-CH_3), 2.05 (s, 3, 17β-Ac), 3.87 (t, 1, J = 5.5 Hz, 2β-H), and 4.67 (t, 1, J = 7.5 Hz, 17α-H).

Hydride Reduction of 3. A mixture of 500 ml of dry ether, 1.27 g (5 mmol) of lithium tri-*tert*-butoxyaluminum hydride, and 1.00 g (3 mmol) of **3** was stirred for 21 hr at room temperature, after which time the excess hydride was destroyed (aqueous ammonium sulfate). The mixture was poured onto water and extracted with ether. Evaporation of the ether gave 1.24 g of an oil, which crystallized upon standing, mp 134–137°. The product appeared to be homogeneous by tlc, and its nmr spectrum indicated it to be the 2α alcohol **14**, contaminated with less than 10% of a mixture of **3**, the 2β epimer **15**, and traces of other materials. (When the reduction was carried out on a smaller scale at 0°, a similar product distribution was observed.) The product was triturated in acetone–hexane and the residue was recrystallized from ether–petroleum ether to give 17β-acetoxy-1β,5β-cyclo-10α-androstan-2α-ol (**14**): mp 138.5–140°; nmr δ 0.80 (s, 3, 18-CH_3), 1.26 (s, 3, 19-CH_3), 2.02 (s, 3, 17β-Ac), and 4.67 (m, 2, 17α-H and 2β-H). *Anal.* Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.77; H, 9.71.

Reoxidation of the reduction mixture with CrO_3–pyridine gave a near-quantitative yield of **3**.

17β-Acetoxy-10α-androst-5-en-2-one (17). One gram of **3** was dissolved in 11 ml of a sulfuric acid–acetic acid solution (1.0 g of 98% sulfuric acid in 100 ml of glacial acetic acid). The resulting solution was heated for 2 hr with stirring at 95° and then cooled in ice and neutralized with 10% aqueous sodium hydroxide solution.

The usual work-up gave a solid (1.05 g) which, in benzene, was filtered through alumina (75 × 13 mm, activity III). The eluent (150 ml) was evaporated to dryness, giving 913 mg of a solid, which was recrystallized from the acetone to give 609 mg of crystals, mp 176–180°. Sublimation at 170° (0.01 mm) gave 576 mg of **17**, mp 180–182° (lit.[9] mp 181–182°). The highest yield obtained in several runs was 64%: ir (Nujol) 1730 (C=O, acetate), 1710 (C=O, ketone), 1250, and 1045 cm^{-1}; nmr δ 0.80 (s, 3, 18-CH_3), 1.05 (s, 3, 19-CH_3), 2.02 (s, 3, 17β-Ac), 4.64 (t, 1, J = 7 Hz, 17α-H), and 5.67 (d, 1, J = 6 Hz, 6-H).

Hydride Reduction of 17. A mixture of 100 ml of dry ether, 300 mg (0.91 mmol) of **17**, and 620 mg (2.44 mmol) of lithium tri-*tert*-butoxyaluminum hydride was stirred at room temperature for 15 hr under nitrogen. The excess hydride was destroyed (aqueous ammonium sulfate) and the usual work-up gave a solid (320 mg). Nmr analysis indicated that the product was primarily the axial 2α-ol **19a**, contaminated with about 20% of the epimeric 2β-ol **19b**.

Repeated chromatography on alumina (130 × 13 mm, activity III) with benzene as eluent gave 212 mg (71%) of 17β-acetoxy-10α-androst-5-en-2α-ol (**19a**), recrystallized from acetone–hexane: mp 206–208°; nmr δ 0.80 (s, 3, 18-CH_3), 1.36 (s, 3, 19-CH_3), 2.03 (s, 3, 17β-Ac), 4.23 (brs, 1, 2β-H), 4.63 (t, 1, J = 7.5 Hz, 17α-H), and 5.46 (d, 1, J = 6 Hz, 6-H). *Anal.* Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.60; H, 9.49. In addition, about 60 mg of predominantly 17β-acetoxy-10α-androst-5-en-2β-ol (**19b**) was isolated. Recrystallization from chloroform–hexane gave **19b**: mp 173–175°; nmr δ 0.81 (s, 3, 18-CH_3), 1.12 (s, 3, 19-CH_3), 2.04 (s, 3, 17β-Ac), *ca.* 4.0 (m, 1, 2α-H), 4.65 (t, 1, J = 7.5 Hz, 17α-H), and 5.46 (d, 1, J = 6 Hz, 6-H). *Anal.* Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.54; H, 9.71.

17β-Acetoxy-5α,10α-androstan-2-one (16a). A mixture of 260 mg of **17**, 80 mg of 5% palladium on charcoal, and 20 ml of absolute ethanol was stirred under 1 atm of hydrogen at room temperature until hydrogen uptake ceased (1 hr). Filtration of the catalyst and evaporation of the solvent gave a solid residue, which on recrystallization from ethanol yielded 238 mg of **16a**: mp 192–195° (lit.[10] mp 194–196°); nmr δ 0.77 (s, 3, 18-CH_3), 0.98 (s, 3, 19-CH_3), 2.03 (s, 3, 17β-Ac), and 4.63 (t, 1, J = 7.5 Hz, 17α-H).

Hydrogenation of 19a. A mixture of 100 mg of **19a**, 25 mg of 5% palladium on charcoal, and 15 ml of absolute ethanol was stirred under 1 atm of hydrogen at room temperature until hydrogen uptake ceased (about 1 hr). Removal of the catalyst and evaporation of the solvent gave a residue which was shown by spectral and chromatographic analysis to be almost completely the 5α product **12a** described above. Hydrolysis of the 17β-acetate group with methanolic sodium hydroxide followed by the usual work-up gave 93 mg of 5α,10α-androstane-2α,17β-diol (**12b**), mp 194–196° (lit.[10] mp 192–195°).

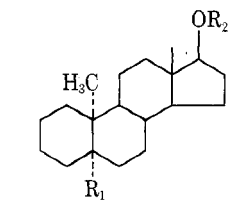
Hydrogenation of 16a. A mixture of 40 mg of **16a**, 20 mg of 5% palladium on charcoal, and 25 ml of absolute ethanol was stirred for 21 hr at 130° under 1550 psig of hydrogen. Removal of the catalyst and evaporation of the solvent gave a residue which was shown by spectral and chromatographic comparisons to be the 2α alcohol **12a**, contaminated by a few per cent of the epimeric 2β alcohol **13a**.

Hydride Reduction of 16a. A mixture of 50 ml of dry ether, 160 mg (0.48 mmol) of **16a**, and 320 mg (1.26 mmol) of lithium tri-*tert*-butoxyaluminum hydride was stirred under nitrogen at room temperature for 16 hr. After the usual work-up 168 mg of material was obtained which was shown by spectral and chromatographic comparisons to be the 2α-hydroxy compound **12a**, contaminated by a trace of **16a** and about 20% of the 2β epimer **13a**. Chromatography of this mixture on activity III alumina with elution first with carbon tetrachloride and then with chloroform gave a pure sample of **13a**, mp 158–161°, from carbon tetrachloride–hexane: nmr δ 0.78 (s, 3, 18-CH_3), 1.02 (s, 3, 19-CH_3), 2.02 (s, 3, 17β-Ac), 3.3 (brm, 1, 2α-H), and 4.62 (t, 1, J = 7.5 Hz, 17α-H). Hydrolysis of this material in methanolic sodium hydroxide gave a solid which on recrystallization from acetone–hexane yielded 5α,10α-androstane-2β,17β-diol (**13b**), mp 210–213° (lit.[10] mp 214–217°).

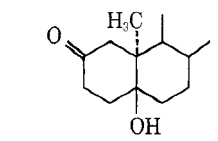
Results and Discussion

Attempted hydrogenolysis of lumitestosterone acetate (**3**) over a palladium catalyst at room temperature and atmospheric pressure gave only recovered starting material from the reaction mixture. Little reaction was observed even when **3** was hydrogenated over palladium at 1500 psig and 70° for 24 hr, but at a temperature of 120–130° a complex mixture of products was obtained which could be reasonably separated by column chromatography.

The infrared spectra of the first three chromatography fractions were very similar with no ketone or hydroxy absorption bands present. The first fraction (A) was shown by glpc analysis to be composed primarily of one compound with two others present in much smaller amounts. The major material was identified as 17β-acetoxy-5α,10α-androstane (**7**) by hydrolysis to the known[9] 5α,10α-androstan-17β-ol (**8**). The minor components were not identified.



7, R_1 = H; R_2 = Ac
8, R_1 = R_2 = H
9a, R_1 = OEt; R_2 = Ac
b, R_1 = OEt; R_2 = H



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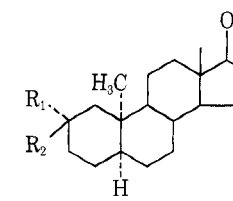
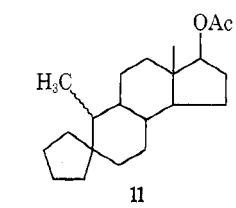


12a, R_1 = OH; R_2 = H; R_3 = Ac
b, R_1 = OH; R_2 = R_3 = H
13a, R_1 = H; R_2 = OH; R_3 = Ac
b, R_1 = H; R_2 = OH; R_3 = H



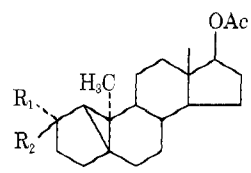
11

The pmr spectrum of the small second fraction (B), which was shown to be homogeneous by chromatographic analysis, indicated the presence of a quaternary ethoxy group in the molecule. Structure **9** was assigned to this material on the basis of spectral and analytical data as well as by analogy with the reported[12] formation of 5α-hydroxy species, **10**, when compounds such as **3** are treated with aqueous acid.

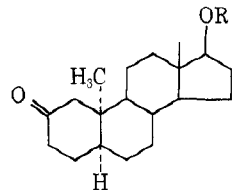
The third fraction (C), which was obtained in very small quantities, was also shown to be homogeneous by chromatographic analysis. Since the pmr spectrum of this material exhibited a doublet for the C_{19} protons with a coupling constant of 7 Hz as is found[13] for compounds such as **11**, this structure was tentatively assigned to this compound. The fourth and major chromatographic fraction (D) was composed primarily of 17β-acetoxy-5α,10α-androstan-2α-ol (**12a**) with about 15% of the 2β-hydroxy epimer **13a** also present. These compounds were identified by hydrolysis to the known[10] 17β alcohols **12b** and **13b**.

As the data in Table I indicate, an increase in the reaction temperature not only increases the amount of cyclopropane hydrogenolysis but it also increases the amount of C_2-deoxy compounds (fraction A) formed. The use of ethyl acetate as the solvent eliminates the formation of **9** and **11** but the distribution of compounds in fractions A and D was essentially the same as that found using ethanol. At lower temperatures in ethyl acetate prolonged hydrogenation gave only a 20% yield of the 2β alcohol **13a**, with 80% of **3** recovered.

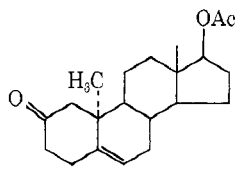
Over Raney nickel in ethanol at 1300 psig and 50–60° the hydrogenation of **3** gave only a 3:1 mixture of the epimeric cyclopropyl carbinols **14** and **15**. The major component of this mixture was assigned the 2α-hydroxy configuration, **14**, by virtue of its identity with the major product obtained by reduction of **3** with lithium tri-*tert*-butoxyaluminum hydride, a reagent which was found[10] to give predominantly the axial 2α alcohol when used to reduce 5α,10α-androstan-3-on-17β-ol (**16b**). This assignment is supported by the chemical shift values for the C_{19} and C_2



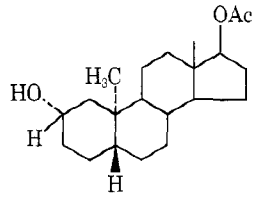
14, R_1 = OH; R_2 = H
15, R_1 = H; R_2 = OH



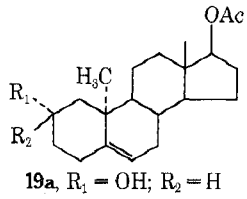
16a, R = Ac
b, R = H



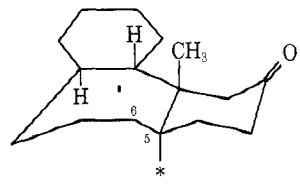
17



18



19a, R_1 = OH; R_2 = H
b, R_1 = H; R_2 = OH



20

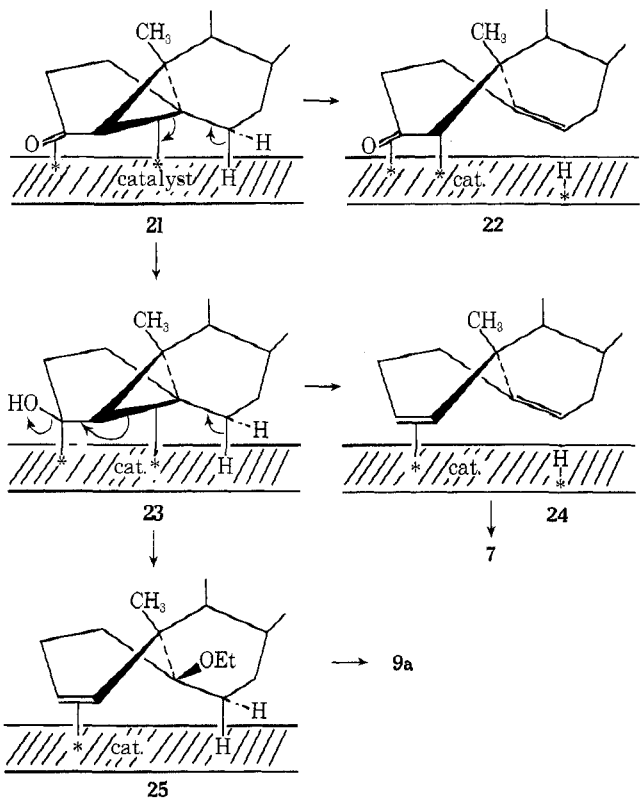
protons of these pairs of alcohols as well as these values for the Δ^5-2-hydroxy compounds, **19a** and **19b**, obtained by the reduction of the ketone **17**.

Hydrogenation of **3** in ethanol over Raney nickel for 24 hr at 1300 psig and 80° gave a more complex mixture of products. This mixture was separated by column chromatography and found to be composed of about 30–35% of **7**, 20% of **9**, 40% of a mixture of **14** and **15**, and 2% of a new alcohol. The pmr spectrum of this material had a singlet for the C_{19} protons at δ 1.30 and a triplet at δ 3.85 (J = 6 Hz) for the C_2 protons. This compound was tentatively assigned the 5β configuration, **18**, but the small amount of material available precluded further characterization.

The marked absence of any appreciable 5β saturated product from the hydrogenolysis of **3** is in direct contrast to the stereoselectivity reported for the hydrogenolysis of other cyclopropyl ketones.[3,4] This difficulty in the formation of the 5β,10α ring fusion is most probably a result of the fact that in this ring system the B ring is forced into a boat conformation,[14] thus providing an added energy barrier to the reaction. In fact, the hydrogenation of either the Δ^5 ketone **17** or alcohol **19a** under a variety of conditions gives exclusive 5α product formation,[15] even though a consideration of molecular models does not clearly show why α adsorption on the catalyst should be so markedly preferred. The facile acid-catalyzed isomerization of **3** to **17**[9] and the almost complete 5α product formation from **3** as well as **17** strongly indicates the intermediacy of a Δ^5 species in the hydrogenolysis of **3**. Since stirring a solution of **3** in ethyl acetate over palladium on charcoal at 140° under 1500 psig of nitrogen for 24 hr effected no change in the substrate, it was apparent that isomerization of **3** to an olefin must be induced during the hydrogenation process.

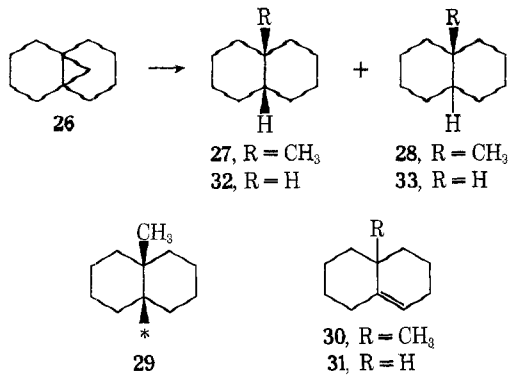
If the 1β,5β bond in **3** is cleaved by the generally accepted mechanism for cyclopropane hydrogenolysis[17] the initial formation of a β-half-hydrogenated state at C_1 or C_5 would be anticipated. The formation of a C_1-half-hydrogenated state would be the result of β-hydrogenation at C_5, something which is not observed. A β-half-hydrogenated state at C_5 (**20**) could then go on to form the C_5–C_6 diadsorbed species, which would be desorbed to give the Δ^5 compound **17**. If this were the case, however, the B ring in **20** would already have at least a semblance of a boat conformation and the energy barrier to boat formation would be essentially passed. It is difficult to see why, under the high hydrogen pressure used in the cleavage of **3**, a simple hydrogen transfer to C_5 did not take place to give at least a moderate amount of the 5β product. The lack of β-hydrogenation with **17** and **19a** is apparently due to the strain imposed on the molecule by the formation of the 5β-half-hydrogenated state or even, possibly, by the 5β,6β-diadsorbed species.

An alternate mechanism for the cleavage of **3** can be proposed, however, in which neither a 5β,6β-diadsorbed species nor a 5β-half-hydrogenated state is involved. The molecular model of **3** shows that the β-C_6 hydrogen bond is directly perpendicular to the 1β,5β bond, the cyclopropane bond which is most accessible to the catalyst surface. This relationship with adsorbed **3** is depicted in **21**. Extraction of this C_6 hydrogen by the catalyst with



concomitant double-bond formation between C_5 and C_6 and cleavage of the C_1–C_5 bond would give the C_1-half-hydrogenated state, **22**. Hydrogen transfer to C_1 and hydrogenation of the adsorbed carbonyl group under the high temperature and pressures used would lead to the 2α-hydroxy-Δ^5 compound **19a**, which would then be readsorbed on the catalyst from the more favored α side to give the observed 5α products. If carbonyl hydrogenation occurred prior to C_6-hydrogen abstraction the adsorbed species, **23**, would be an intermediate. Dehydration of **23** could occur along with C_1–C_5 bond cleavage to give a diolefin, **24**, which could be saturated to give the 2-deoxy-5α products observed. α- attack by ethanol at C_5 of **23** followed by breaking the C_1–C_5 bond and loss of the OH group would lead, after saturation of the Δ^2 olefin, to **9a**.

Support for this proposal comes from a consideration of the data obtained on the hydrogenolysis of tricyclo[4.4.1.0]undecane (**26**).[2] Hydrogenolysis of **26** over platinum in acetic acid at 50 psig and 55° gives nearly equal amounts of the *cis*- and *trans*-9-methyldecalins (**27** and **28**). If direct cyclopropane bond cleavage had occurred through the intermediacy of the cis-half-hydrogenated



state, **29**, predominant formation of the cis decalin **27** would be expected. As shown for **3** in diagram **21**, the C_1 equatorial hydrogen bond in **26** is perpendicular to the cyclopropane bond which is adsorbed on the catalyst. Thus, the formation of the olefin **30** could occur by a process similar to that described for the formation of **22**. While the product stereochemistry obtained from the hydrogenation of **30** is not available, it has been reported that the hydrogenation of the demethyl compound **31** over platinum in acetic acid at room temperature and 1 atm gives a 60:40 mixture of the cis and trans decalins **32** and **33**.[18] Further work is currently underway in an attempt to establish whether the hydrogenolysis of cyclopropyl compounds such as **3** and **26** does, indeed, take place through an olefin intermediate as proposed here.

Registry No.—**3**, 2506-66-3; **7**, 51267-72-2; **9a**, 51231-35-7; **9b**, 51231-36-8; **11**, 51231-37-9; **12a**, 26605-74-3; **13a**, 51267-73-3; **14**, 51231-38-0; **16a**, 5986-74-3; **17**, 21496-61-7; **18**, 51267-74-4; **19a**, 26606-26-8; **19b**, 51231-39-1.

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Selective Reductions. XX. Stereochemistry of the Reduction of Cyclic, Bicyclic, and Polycyclic Ketones by Dialkylboranes. A Simple, Convenient Procedure for the Reduction of Ketones to the Corresponding Alcohols with Exceptionally High Steric Control[1]

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The introduction of two alkyl substituents into borane provides a simple, convenient means of modifying the steric requirements and reducing properties of this reagent. Dialkylboranes are found to be consistent reagents for steric control of reduction in monocyclic, bicyclic, and steroidal systems. 2-Alkylcycloalkanones of various ring size are reduced to 2-alkylcycloalkanols to give predominantly the less thermodynamically stable of the two possible alcohols (cis). In the case of bicyclic and steroidal ketones, which are analogs of 2-alkylcyclohexanones (such as 1-, 4-, or 6-keto steroids), dialkylboranes provide the less stable of the two possible alcohols in high isomeric purity. Unlike the conventional reagents, such as lithium aluminum hydride, borane, etc., the remarkable consistency exhibited by dialkylboranes in directing the reduction of these ketones from the less hindered direction provides a simple, convenient method for distinguishing the less hindered side of the molecule and for establishing the configurations of a pair of epimeric alcohols. Dialkylboranes provide the basis for a highly convenient synthetic procedure to achieve steric control of reduction of cyclic ketones where such control is required in synthetic operations such as the essentially quantitative conversion of 2-cyclohexylcyclohexanone to *cis*-2-cyclohexylcyclohexanol in 96% stereochemical purity.

The stereochemistry of the reduction of cyclic ketones by complex metal hydrides and metal hydrides has attracted considerable attention, both from the synthetic as well as mechanistic viewpoint.[3] These extensive studies, in addition to providing simple procedures for the stereoselective synthesis of alcohols, have resulted in many fundamental theoretical concepts concerning nucleophilic additions to the carbonyl group. Since their discovery, the complex metal hydrides, such as lithium aluminum hydride and sodium borohydride, have been widely utilized for the conversion of ketones to alcohols. However, there is a major disadvantage in applying these reagents to cyclic ketones. Thus, reduction of cyclic ketones such as 2-methylcyclohexanone with lithium aluminum hydride appears