tained no bands characteristic of lactone **3**. In order to determine if lactone **3** could have been an intermediate in the formation of **4**, the zinc acetate catalyzed reaction was carried out with **3** initially present. During reaction the lactone was not consumed and was recovered by distillation from the reaction mixture. In this reaction, then, the polyester was not formed by polymerization of an intermediate $\beta$-lactone, but must have arisen by a process not involving the lactone.

Although the mechanism for the direct conversion of ketene and aldehydes to polyesters in the presence of zinc carboxylic acid salts is unknown at present, it is interesting to note that zinc acetate is probably not acting as a Lewis acid. In the reaction of ketene with acrolein (eq 1), boron trifluoride, a strong Lewis acid, leads to $\beta$-lactone formation, whereas zinc acetate leads to formation of the polyester. Also, *n*-butylzinc and ethyl bromozinc acetate when used as catalysts give as high a yield of polyester as does zinc acetate.

An interesting mechanistic possibility for this reaction involves the insertion of ketene into the zinc catalyst to form a zinc alkyl compound.[7] The zinc alkyl could then add to a molecule of aldehyde, as in the Reformatsky reaction, to give a zinc alkoxide. Insertion of ketene into the zinc alkoxide would re-form a zinc alkyl species which could continue the polymerization.[8]

### Experimental Section

Boiling points are uncorrected. The ir spectra were obtained with a Baird-Atomic Model AB-2 spectrometer using sodium chloride cells. Nmr spectra were determined at 60 MHz with Varian Associates A-60 spectrometers. Field position values are recorded in parts per million relative to tetramethylsilane as an internal standard. Nmr peak multiplicities are abbreviated as follows: s (singlet), d (doublet), t (triplet), dd (doublet of doublets), and m (multiplet). Mass spectra were recorded on an AEI Model MS 902 spectrometer. Molecular weights were determined by vapor phase osmometry by European Research Associates, Union Carbide Corp.

**Poly(3-hydroxy-4-hexenoic acid) (1).**—To a 5-l. four-necked reaction flask equipped with a stirrer, thermometer, condenser, and ketene diffuser were added crotonaldehyde (1260 g, 18.0 mol), toluene (2400 cc), and zinc isovalerate (13.5 g). Ketene (662 g, 15.7 mol) was added over a period of 6 hr while the temperature was maintained at 25°. During this time only 3 g of ketene came through the reaction zone unchanged. The reaction mixture was purged with nitrogen for 15 min, then stripped of solvent and excess crotonaldehyde under vacuum. The polyester, obtained as a residue from the distillation, weighed 1576 g (90% based on ketene): mol wt, 1200; ir (neat) 5.75 (C=O), 8.06 (COOC), and 10.43 $\mu$ (C=C); nmr ($CDCl_3$) 1.68 (d, 3, $J$ = 6 Hz, $CHCH_3$), 2.61 (d, 2, $J$ = 7 Hz, $CH_2CO$), and 5.6 ppm (m, 3).

**Reduction of 1.**—To a stirred suspension of lithium aluminum hydride (10.6 g) in ethyl ether (650 cc) was added a solution of **1** (50 g) in ethyl ether (250 cc) at a rate such that gentle reflux was maintained. After complete addition, the mixture was stirred for 2 hr, then quenched with water (25 cc). The ether solution was clarified by filtration, dried over magnesium sulfate, and distilled through a 7-in. glass helix column to give 32 g (62%) of 4-hexene-1,3-diol: bp 82–85° (1 mm); ir (neat) 2.9 (O–H) and 5.92 $\mu$ (C=C); nmr ($CDCl_3$) 1.72 (d, 3, $J$ = 4 Hz, $CH_3$), 1.70 (m, 2, $CH_2$), 3.69 (t, 2, $J$ = 5 Hz, $CH_2OH$), 4.20 (m, 1, CHOH), 4.52 (s, 2, OH), and 5.56 ppm (m, 2, HC=CH). The mass spectrum of this material possessed a parent molecular ion at $m/e$ 116.0833 ($C_6H_{12}O_2$ required 116.0837).

*Anal.* Calcd for $C_6H_{12}O_2$: C, 62.07; H, 10.35. Found: C, 62.30; H, 10.38.

(7) For similar reactions, see L. C. Willemsens and G. J. M. van der Kerk, *J. Organometal. Chem.*, **4**, 241 (1965); I. F. Lutsenko, V. L. Foss, and N. L. Ivanova, *Dokl. Akad. Nauk SSSR*, **141**, 1270 (Engl) (1961).

(8) M. F. Lappert and B. Prokai, *Advan. Organometal. Chem.*, **5**, 242 (1967).

**4-Hexene-1,3-diol.**—Ethyl 3-hydroxy-4-hexenoate was prepared in 60% yield by the Reformatsky reaction of ethyl bromozinc acetate with crotonaldehyde under the conditions described by Fischer and Löwenberg.[9] The hydroxy ester (26 g, 0.16 mol) was reduced with lithium aluminum hydride (5.95 g, 0.156 mol) in ethyl ether giving 15 g (79%) of 4-hexene-1,3-diol, bp 80–85° (2 mm). The sample was identical (vpc, ir, nmr) with that obtained above. The mass spectrum of this material possessed a parent molecular ion at $m/e$ 116.0840 ($C_6H_{12}O_2$ required 116.0837).

**Attempted Preparation of 2.**—A four-necked 500-cc reaction flask equipped with a stirrer, thermometer, condenser, diffusion tube, and dropping funnel was charged with dry toluene (250 cc) and boron trifluoride etherate (4 cc). To this was simultaneously added ketene (60 g, 1.4 mol) and crotonaldehyde (70 g, 1.0 mol); the temperature was maintained at −25°. After complete reaction, the catalyst was destroyed with sodium acetate (3.5 g), and the nmr spectrum of the cold solution was scanned. The nmr spectrum contained no absorption bands in the region between 3 and 4 ppm, the area in which hydrogens $\alpha$ to the carbonyl group of $\beta$-lactones absorb.

**Preparation of 3.**—The apparatus and procedure were the same as used in the attempted preparation of **2**. Acrolein (56 g, 1.0 mol) and ketene (59 g, 1.4 mol) were simultaneously added to the boron trifluoride solution at −25°. Destruction of the catalyst and distillation gave 71 g (72%) of **3**: bp 44–48° (4 mm) [lit.[6] bp 45–50° (3 mm)]; ir (neat) 5.4 ($\beta$-lactone C=O) and 8.0 $\mu$ (COOC); nmr (neat) 3.18 (dd, 1, C(=O)CH), 3.69 (dd, 1, C(=O)CH), 5.3 (m, 3), and 6.11 ppm (m, 1, O—CH).

**Preparation of 4 in the Presence of 3.**—A solution of acrolein (100 g), **3** (40 g), and zinc isovalerate (1 g) in benzene (150 cc) was charged into a four-necked 500-cc reaction flask equipped with a stirrer, thermometer, gas diffuser, and condenser. Ketene (70 g) was passed into the solution, but only a fraction of this (14 g) was absorbed. The reaction mixture was purged with nitrogen and distilled. Besides solvent and acrolein, there was obtained lactone **3** (27 g) and residue (22 g). Analysis of the nmr spectrum of the crude reaction mixture indicated that 36 g of **3** was present prior to distillation.

**Registry No.**—Ketene, 463-51-4; 4-hexene-1,3-diol, 24655-66-1; **3**, 7379-74-0.

(9) F. G. Fischer and K. Löwenberg, *Chem. Ber.*, **66**, 669 (1933).

## Routes to 2,19-Oxido-$\Delta^{4,6}$-3-keto Steroids

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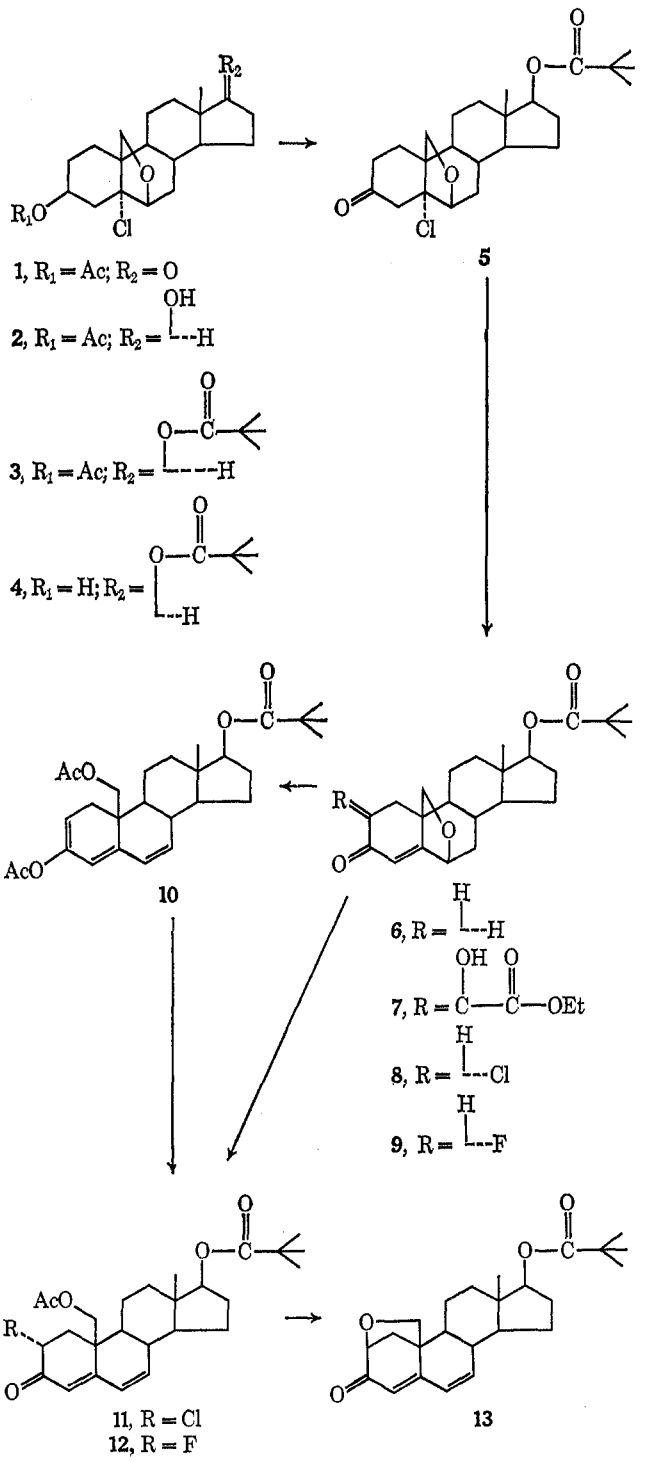
Saturated 2,19-oxido-3-keto steroids have recently been prepared from the corresponding 2$\beta$-hydroxy-3$\alpha$-acetates.[1] Attempts to convert these ketones into their conjugated analogs[1b] failed, however, and the steric deformation induced by the 2,19-oxide bridge has been made responsible for this. We wish to report the preparation of 2,19-oxido-4,6-dien-3-one (**13**) from 2-halo-19-acetoxy-$\Delta^{4,6}$-3-ketones **11** and **12** by hydrolysis and concomitant substitution of the halogen atoms in position 2 by the liberated 19-hydroxy group.

The synthesis commenced with 3$\beta$-acetoxy-5$\alpha$-chloro-6,19-oxidoandrostan-17-one (**1**).[2] In view of the subsequent halogenating reactions planned, it appeared desirable to protect the oxygen function in position 17 by an ester group. The pivalate was chosen, as it

(1) (a) R. Kwok and M. E. Wolff, *J. Org. Chem.*, **28**, 423 (1963); (b) M. E. Wolff, W. Ho, and R. Kwok, *Steroids*, **5**:1, 1 (1964).

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

allowed for a selective hydrolysis of the 3-acetate. The 17-keto group of **1** was reduced with sodium borohydride to the 17$\beta$-alcohol **2**, which gave **3** on heating with pivaloyl chloride in pyridine. Base-catalyzed hydrolysis in methanol gave the 3$\beta$-alcohol **4**, which on oxidation with chromic acid in acetone and subsequent treatment of the reaction product **5** with pyridine gave $\Delta^4$-3-ketone **6**. The 2-chloro derivative **8** was prepared *via* ethoxalyl derivative **7** by a modification of the method of Yasuda.[3] Treatment of the ethoxalyl derivative with perchloryl fluoride in methanolic sodium carbonate[4] gave the 2-fluoro-$\Delta^4$-3-ketone **9**. The conversion of 2-halo-6,19-oxides **8** and **9** to $\Delta^{4,6}$-3-ketones **11** and **12** was achieved by heating the two oxides in acetic anhydride in the presence of *p*-toluenesulfonic acid. Considerably more *p*-toluenesulfonic acid was required for the effective opening of the oxide ring of the 2-halo-3-ketones **8** and **9** than has been found necessary for the opening of the oxide ring of ketone **6** under comparable conditions.[5] Both the 2-chloro-$\Delta^{4,6}$-3-ketone **11** and the 2-fluoro analog **12** gave readily the 2,19-oxide **13** on treatment of their methanolic solutions with excess base at room temperature or on refluxing of the methanolic solutions with aqueous hydrochloric acid. At no time during the hydrolysis could the formation of a free 19-alcohol be observed as indicated by tlc.




In another route, 6,19-oxido-$\Delta^4$-3-ketone **6** was converted into 3-acetoxy-2,4,6-triene **10** by treatment with isopropenyl acetate and *p*-toluenesulfonic acid.[6] Selective chlorination at position 2 with calcium hypochlorite gave **11** and hence **13** as before. Non-reductive ring opening of 6,19-oxido-$\Delta^4$-3-keto steroids has previously been accomplished with acetic anhydride in presence of *p*-toluenesulfonic acid and the corresponding 19-acetoxy-$\Delta^{4,6}$-3-ketones were obtained.[7]

The $\alpha$ position has been assigned to the halogen atoms in $\Delta^{4,6}$-3-ketones **11** and **12** as then the ease of the 2,19-oxide formation could readily be explained by an intramoleular SN2 mechanism in which the $\beta$-orientated 19-hydroxy group substitutes the $\alpha$-halogen atoms by rear attack on carbon atom 2. The $\alpha$ position of the halogen atoms of compounds **8**, **9**, **11**, and **12** has also been established by comparison of their ir,[3] uv,[3] and nmr[8] spectra with those of previously prepared analogs. The 2,19-oxide bridge in **13** is confirmed by comparison of its nmr spectrum with those of previously prepared 2,19-oxido steroids.[9]

## Experimental Section[10]

**6,19-Oxido-17$\beta$-pivaloxyandrost-4-en-3-one (6).**—To a solution of 10 g of 1[2] in 300 ml of methanol was added at 0° 0.80 g of sodium borohydride over 2 min with stirring. After being stirred for 30 min in an ice bath, the mixture was poured into 300 ml of 2 *N* aqueous sulfuric acid. The precipitate was filtered off, washed well with water, and dried at 80° under high vacuum for 16 hr yielding 9.0 g of **2** as indicated by tlc.

A stirred mixture of 2 g of 17 alcohol **2**, 10 ml of pyridine, and 2 ml of pivaloyl chloride was slowly heated to 100° during 1 hr and kept at this temperature for 30 min. The mixture was then poured into 50 ml of water with stirring. The precipitate of crude **3** was filtered off, washed well with water, and dried at 50° under high vacuum for 16 hr. The total crude product of **3** was then suspended in 20 ml of methanol and stirred with 0.1 g of potassium hydroxide at room temperature for 2 hr. The sus-

(3) K. Yasuda, *Chem. Pharm. Bull.*, **12**, 1217 (1964).

(4) C. Djerassi, "Steroid Reactions," Holden-Day Inc., San Francisco, Calif., 1963, pp 165–166.

(5) G. Kruger, unpublished work.

(6) D. J. Marshall, unpublished results, has prior to us used this method for the ring opening of the 17-ketone and the 17$\beta$-benzoxy analogs of **6**. We are indebted to Dr. Marshall for providing us with the experimental details of this novel and rather cleanly proceeding reaction.

(7) K. Heusler, J. Kalvoda, Ch. Meystre, H. Ueberwasser, P. Wieland, J. Anner, and A. Wettstein, *Experientia*, **18**, 464 (1962).

(8) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, pp 46–52.

(9) Reference 8, pp 69–73.

(10) Melting points were determined with a Thomas–Hoover apparatus and are corrected. Ir spectra were determined with a Perkin-Elmer spectrophotometer, Model 21. Nmr spectra were determined in deuteriochloroform with a Varian A-60 spectrometer; chemical shifts are reported in parts per million downfield from tetramethylsilane.

pension was neutralized with 0.15 ml of glacial acetic acid and diluted with 20 ml of water. Filtration and washing with water gave 1.6 g of crude 3-alcohol **4**.

To a solution of 1.0 g of **4** in 10 ml of acetone was added 2.0 ml of 50% aqueous chromic acid over 1 hr with stirring, whereupon the mixture was poured into 100 ml of water. The precipitate of crude **5** was filtered off, washed well with water, and dried over calcium chloride overnight. It was then refluxed with 2 ml of pyridine for 15 min. Dilution with water and filtration gave 0.80 g of crude **6** which was purified by recrystallization from methanol: mp 157–158°; $\lambda_{max}^{EtOH}$ 238 mμ (ε 14,320); $\nu_{max}^{CHCl_3}$ 1715 (pivalate) and 1776 cm$^{-1}$ (Δ$^4$-3-ketone); the nmr spectrum showed maxima for 1 olefinic proton as a singlet at 5.80 (4 position), 2 protons as a multiplet between 4.4 and 4.8 (6 and 17 position), 2 methylenic protons as a quartet ($J$ = 8 Hz, $\delta_A - \delta_B$ = 0.70 ppm) centered at 3.85 (19 position), 9 protons as a singlet at 1.21 (pivalate), and 3 protons as a singlet at 0.90 ppm (18 position).

*Anal.* Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87. Found: C, 74.69; H, 8.73.

**2-Ethoxalyl-6,19-oxido-17β-pivaloxyandrost-4-en-3-one (7).**—A mixture of 8 g of **6**, 8 g of 54% sodium hydride (dispersed with mineral oil), 8 ml of benzene (dried over sodium hydride), and 8 ml of diethyl oxalate was stirred under nitrogen at room temperature for 3 hr after which time a vigorous reaction set in necessitating cooling. After 4 hr the reaction mixture, which had thickened considerably, was treated with 400 ml of hexane and 200 ml of partially frozen 1 *N* aqueous hydrochloric acid. A yellow precipitate formed which was filtered off, washed with hexane and with water, and dried over calcium chloride yielding 9.5 g of crude **7**: tlc on silica gel with ethyl acetate–benzene (1:4) showed only a single extended spot and no starting material; $\nu_{max}^{CHCl_3}$ 1620 cm$^{-1}$ (strong, –COC=COH–?) in addition to strong carbonyl bands around 1720 cm$^{-1}$.

**2α-Chloro-6,19-oxido-17β-pivaloxyandrost-4-en-3-one (8)** was prepared from crude **7** by the method of Yasuda[8] using pyridine and 1.2 mol of N-chlorosuccinimide. Recrystallization from methanol yielded the pure sample: mp 209–212°; $\lambda_{max}^{EtOH}$ 240 mμ (ε 13,500); $\nu_{max}^{CHCl_3}$ 1720 (pivalate) and 1690 cm$^{-1}$ (2α-chloro-Δ$^4$-3-ketone).

*Anal.* Calcd for $C_{24}H_{33}O_4Cl$: C, 68.46; H, 7.92. Found: C, 68.28; H, 7.61.

**2α-Fluoro-6,19-oxido-17β-pivaloxyandrost-4-en-3-one (9).**—A mixture of 2.0 g of **7** and 0.43 g of sodium carbonate in 20 ml of methanol was heated at 60° under nitrogen until all material had dissolved. The solution was cooled to 0° and then treated with a fine stream of perchloryl fluoride gas for 3 min, whereupon it was boiled under nitrogen for 5 min. Addition of water followed by recrystallization of the precipitate from methanol gave 0.6 g of the analytical sample: mp 218–219.5°; $\lambda_{max}^{EtOH}$ 238 mμ (ε 15,300); $\nu_{max}^{CHCl_3}$ 1715 (pivalate) and 1695 cm$^{-1}$ (2α-fluoro-Δ$^4$-3-ketone, overlaps with peak at 1715 cm$^{-1}$). The nmr spectrum showed maxima for 1 olefinic proton as a doublet ($J$ = 4 Hz) centered at 5.85 (4 position), 0.5 proton as a pair of doublets ($J_{2\beta,1\alpha}$ = 14, $J_{2\beta,1\beta}$ = 6 Hz)[11] centered at 5.35 (2β position), 2.5 protons as a multiplet between 4.38 and 4.90 (6 and 17 positions with the remaining 0.5 2β proton, $J_{2\beta,F} \approx 45$ Hz),[11] 2 methylenic protons as a quartet ($J$ = 8 Hz, $\delta_A - \delta_B$ = 0.65 ppm) centered at 3.89 (19 position), 9 protons as a singlet at 1.19 (pivalate), and 3 protons as a singlet at 0.89 ppm (18 position).

*Anal.* Calcd for $C_{24}H_{33}O_4F$: C, 71.3; H, 8.21. Found: C, 71.13; H, 8.31.

**3,19-Diacetoxy-17β-pivaloxyandrosta-2,4,6-triene (10).**—A solution of 20 g of 6,19-oxido-17β-pivaloxyandrost-4-en-3-one (**6**) in 40 ml of isopropenyl acetate was refluxed in presence of 2 g of *p*-toluenesulfonic acid for 2 hr under nitrogen, whereupon it was extracted five times with 50 ml of water, dried with sodium sulfate, and evaporated at reduced pressure. The crystalline residue was recrystallized from methanol yielding 4.1 g of the analytical sample: mp 147–148°; $\nu_{max}^{CHCl_3}$ 1725–1750 (broad, >C=O) and 1670 cm$^{-1}$ (>C=C<); $\lambda_{max}^{MeOH}$ 300 mμ (ε 14,250); the nmr spectrum showed maxima for 2 olefinic protons as an octet (ABX system; $J_{AB}$ = 10, $J_{AX}$ = 2, $J_{BX}$ = 1.5 Hz) centered at 5.86 (6 and 7 position), 1 olefinic proton as a singlet at 5.55 (4 position), 1 olefinic proton as a multiplet between 5.18 and 5.48 (2 position), 1 proton as a broad triplet between 4.4 and 4.8 (17 position), 2 methylenic protons as a quartet ($J$ = 11 Hz, $\delta_A - \delta_B$ = 0.20 ppm) centered at 4.20 (19 position), 1 proton as a pair of doublets (AMX system) centered at 2.70 (1β position, $J_{1\beta,2\beta}$ = 6 Hz), 3 protons as a singlet at 2.13 (enolic 3-acetate), 3 protons as a singlet at 2.03 (19-acetate), 9 protons as a singlet at 1.20 (pivalate), and 3 protons as a singlet at 0.85 ppm (18 position).

*Anal.* Calcd for $C_{28}H_{38}O_6$: C, 71.46; H, 8.14. Found: C, 71.56; H, 8.01.

**2α-Chloro-17β-pivaloxy-19-acetoxyandrosta-4,6-dien-3-one (11). Method A.**—A mixture of 4.60 g of **8**, 23 ml of acetic anhydride, and 4.6 g of *p*-toluenesulfonic acid was heated at 100° for 10 min under nitrogen, whereupon the mixture was cooled and poured in a fine stream into 115 ml of cold methanol saturated with ammonia. The solution was concentrated to approximately 20 ml and water was added yielding, after filtration of the precipitate formed and drying, 4.2 g of crude **11**, $\lambda_{max}$ 285 mμ, which by tlc was identical with the pure product prepared by method B and which was used for the preparation of 2,19-oxide **13**.

**Method B.**—A solution of 13 g of **10** in 26 ml of benzene was shaken with a solution of 49 ml of acetic acid and 13 g of calcium hypochlorite in 2600 ml of water for 3 min at room temperature. Extraction of the benzene phase with water, followed by evaporation and recrystallization of the residue from methanol, gave 2.0 g of the analytically pure material: mp 95–141°; $\lambda_{max}^{EtOH}$ 285 mμ (ε 25,800); $\nu_{max}^{CHCl_3}$ 1745 (acetate), 1720 (pivalate), 1680 (conjugated ketone), 1625 and 1595 cm$^{-1}$ (>C=C<). The nmr spectrum showed maxima for 2 olefinic protons as a singlet at 6.16 (6 and 7 positions), 1 olefinic proton as a singlet at 5.92 (4 position), 1 proton as a pair of doublets (AMX system) centered at 4.93 ($J_{2\beta,1\alpha}$ = 13, $J_{2\beta,1\beta}$ = 6 Hz; 2β position), 1 proton as a broad triplet between 4.40 and 4.75 (17 position), 2 methylenic protons as a quartet ($J$ = 12 Hz, $\delta_A - \delta_B$ = 0.22 ppm), centered at 4.31 (19 position), 1 proton as a pair of doublets centered at 2.85 ($J_{1\beta,1\alpha}$ = 12, $J_{1\beta,2\beta}$ = 6 Hz; 1β position), 3 protons as a singlet at 2.05 (acetate), 9 protons as a singlet at 1.22 (pivalate), and 3 protons as a singlet at 0.90 ppm (18 position).

*Anal.* Calcd for $C_{26}H_{35}O_5Cl$: C, 67.60; H, 7.63; Cl, 7.86. Found: C, 67.64; H, 7.80; Cl, 7.66.

**2α-Fluoro-Δ$^{4,6}$-3-ketone 12** was obtained from **9** as an oil ($\lambda_{max}$ 284 mμ) by the ring-opening procedure above used for the preparation of **11** from **8**. It was not further purified but used for the next reaction.

**2,19-Oxido-17β-pivaloxyandrosta-4,6-dien-3-one (13).**—A solution of 0.72 g of potassium hydroxide and 3.6 g of crude **11** in 72 ml of methanol was left to stand at room temperature for 1 hr, whereupon 1 ml of glacial acetic acid was added. The methanol was removed at reduced pressure, and the residue dissolved in a mixture of ethyl acetate and water. The organic phase was treated with charcoal, filtered, and dried with sodium sulfate yielding, after evaporation and digestion of the residue with methanol, 1.8 g of crystalline 2,19-oxide **13**. Recrystallization from methanol yielded the pure product: mp 171.5–172.5°; $\lambda_{max}^{EtOH}$ 285 mμ (ε 26,880); $\nu_{max}^{CHCl_3}$ 1715 (pivalate), 1670 (Δ$^{4,6}$-3-ketone), 1615 and 1575 cm$^{-1}$ (>C=C<); the nmr spectrum showed maxima for 2 olefinic protons as a singlet at 6.20 (6 and 7 positions), 1 olefinic proton as a doublet ($J$ = 2 Hz) centered at 5.72 (4 position), 1 proton as a broad triplet between 4.50 and 4.85 (17 position), 1 proton as a pair of doublets (AMX system) centered at 4.34 ($J_{2\alpha,1\beta}$ = 6, $J_{2\alpha,1\alpha}$ = 2 Hz; 2α position), 2 methylenic protons as a quartet ($J$ = 8 Hz, $\delta_A - \delta_B$ = 0.45 ppm) centered at 3.82 (19-position), one proton as a pair of doublets centered at 2.39 ($J_{1\beta,1\alpha}$ = 11.5, $J_{1\beta,2\alpha}$ = 6 Hz; β position), 9 protons as a singlet at 1.20 (pivalate), and 3 protons as a singlet at 0.85 ppm (18 position).

*Anal.* Calcd for $C_{24}H_{32}O_4$: C, 74.95; H, 8.39. Found: C, 74.91; H, 8.11.

Crude 2-fluoro-Δ$^{4,6}$-3-ketone **12**, when subjected to alkaline hydrolysis as above, yielded a crystalline product which had an ir spectrum identical with that of 2,19-oxide **13**.

When a solution of 100 mg of 2-chloro-19-acetate **11** in 2 ml of 4 *N* aqueous hydrochloric acid–methanol (1:5) was refluxed for 6 hr, working up and recrystallization from methanol yielded 8 mg of a product, mp 169–171°, which by tlc was identical with the fully characterized 2,19-oxide **13** prepared above. 2-Fluoro analog **12** also yielded **13** when subjected to the same acidic hydrolysis conditions as evidenced by tlc.

**Registry No.**—**6**, 24099-40-9; **7**, 24099-41-0; **8**, 24099-42-1; **9**, 24099-43-2; **10**, 24099-44-3; **11**, 24099-45-4; **13**, 24099-46-5.

(11) Reference 8, p 148.

**Acknowledgment.**—The authors are indebted to Dr. G. Schilling, Mr. M. Boulerice, and Mrs. J. Jachner for nmr, ultraviolet, and infrared spectra and to Mr. W. Turnbull and Miss E. Wieslander for microanalyses. We would also like to thank Dr. G. S. Myers for generous supplies of starting material.

## Preparation of Some $\Delta^{4,7}$- and $\Delta^{1,4,7}$-3-Keto Steroids by Deconjugation

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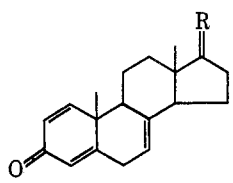
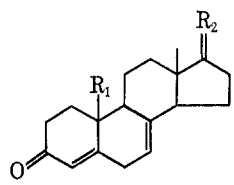
Deconjugation of unsaturated ketones can be achieved by deprotonation with strong bases followed by acid treatment of the enolate anions formed. Thus Ringold and Malhotra[1] have recently deconjugated steroidal $\Delta^4$-3-ketones to the corresponding $\Delta^5$-3-ketones, using potassium *t*-butoxide in *t*-butyl alcohol for the deprotonation and aqueous acetic acid for the subsequent protonation, while Shapiro, Legatt, Weber, and Olivetto[2] converted $\Delta^{1,4}$-3-ketones into the corresponding $\Delta^{1,5}$-3-ketones using basic reagents, such as potassium *t*-butoxide, sodium acetylide, sodium amide, and sodium hydride, in aprotic solvents for the deprotonation and weak acids such as acetic acid and boric acid for the subsequent protonation. In some of their experiments the authors used potassium *t*-butoxide as the base and dimethyl sulfoxide as the aprotic solvent. We wish to report the preparation of some $\Delta^{4,7}$- and $\Delta^{1,4,7}$-3-ketones by treatment of the fully conjugated ketones with sodium methoxide in dimethyl sulfoxide and subsequent reprotonation with strong aqueous acids, such as aqueous 2 *N* hydrochloric acid. When weak acids were used for the final protonation inferior yields of the desired $\Delta^{4,7}$- or $\Delta^{1,4,7}$-3-ketones were obtained and this was attributed to the intermediate formation of the isomeric $\Delta^{5,7}$- and $\Delta^{1,5,7}$-3-ketones. Thus, when in the deconjugation of 17$\beta$-hydroxyandrosta-4,6-dien-3-one the basic mixture was poured into aqueous 2 *N* acetic acid, ultraviolet analysis on the ether extract showed two sharp absorption peaks at 270 and 275 m$\mu$ which were considered to derive from 17$\beta$-hydroxyandrosta-5,7-dien-3-one and which disappeared on shaking the ether extract with 2 *N* aqueous hydrochloric acid with concomitant increase in absorption at 239 m$\mu$, indicating additional formation of the desired $\Delta^{4,7}$-3-ketone.

Generally, the conjugated ketones were treated with two parts of sodium methoxide in ten parts of dimethyl sulfoxide at room temperature and in an atmosphere of nitrogen. The basic reaction mixture was poured into excess 2 *N* hydrochloric acid; ultraviolet analysis on a small sample of reaction mixture, acidified with 2 *N* hydrochloric acid, indicated the presence of only trace amounts of starting material. For the isolation of **4** in the pure form it was found necessary to resort to chromatography.

The preparation of **4** has previously been achieved[3] by allylic bromination of the ethylene ketal of testosterone benzoate, dehydrobromination to the corresponding 5,7-diene, alkaline hydrolysis of the benzoate in the 17 position, and acid hydrolysis of the 3-ketal with dilute sulfuric acid in alcohol, while **3** has been prepared[4] by conversion of 17$\beta$-hydroxy-4,6-estradiene-3,17-dione into the corresponding 3,17$\beta$-diacetoxy-3,5,7-triene, sodium borohydride reduction to the 3$\beta$,17-dihydroxy-5,7-diene, and subsequent Oppenauer oxidation.



**1**, R = O
**2**, R = OH
---H



**3**, $R_1$ = H; $R_2$ = O
**4**, $R_1$ = Me; $R_2$ = OH
---H

### Experimental Section[5]

**1,4,7-Androstatriene-3,17-dione** (1).—To a solution of 10.0 g of 1,4,6-androstatriene-3,17-dione[6] in 100 ml of dimethyl sulfoxide, 20 g of sodium methoxide was added in one portion. The mixture was stirred for 5 min in an atmosphere of nitrogen and then poured into a stirred solution of 600 ml of ice-cold, aqueous 2 *N* hydrochloric acid. Filtration and recrystallization of the precipitate from methanol–ethyl acetate (1:1) gave 5.5 g of 1,4,7-androstatriene-3,17-dione, mp 160–170°. Two further recrystallizations gave material of mp 168–170° (softening at 161°), $\lambda_{max}^{EtOH}$ 241 m$\mu$ ($\epsilon$ 15,800), $\nu_{max}^{CHCl_3}$ 1735 and 1663 cm$^{-1}$ (17- and 3-ketones). The nmr spectrum showed maxima for 4 olefinic protons as multiplets between 6.0 and 7.3 (1, 2, and 4 positions) and 5.3 and 5.6 (7 position), 2 allylic protons (6 position) as a multiplet between 2.8 and 3.8, 3 protons (19 position) as a singlet at 1.28, and 3 protons (18 position) as a singlet at 0.82 ppm.

*Anal.* Calcd for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.56; H, 7.99.

**17$\beta$-Hydroxy-1,4,7-androstatrien-3-one** (2) was prepared as above in 60% yield from 17$\beta$-hydroxy-1,4,6-androstatrien-3-one[6] or from the 17-acetate, which was completely hydrolyzed under the reaction conditions: mp 185–186°; $\lambda_{max}^{EtOH}$ 242 m$\mu$ ($\epsilon$ 17,800); $\nu_{max}^{CHCl_3}$ 3,640 (OH), 3450 (OH), and 1661 cm$^{-1}$ (3-ketone). The nmr spectrum showed maxima for 4 olefinic protons as multiplets between 6.0 and 7.2 (1, 2, and 4 positions) and 5.15 and 5.4 (7 position), 1 proton as a broad triplet between 3.6 and 3.95 (17 position), 2 protons (6 position) as a multiplet between 2.8 and 3.5, 3 protons as a singlet at 1.25 (19 position), and 3 protons as a singlet at 0.70 ppm (18 position).

*Anal.* Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.13; H, 8.21.

**4,7-Estradiene-3,17-dione** (3) was prepared as above in 46% yield from 4,6-estradiene-3,17-dione,[4] mp 147–148° (lit.[4] mp 148–149°), $\lambda_{max}^{EtOH}$ 238 m$\mu$ ($\epsilon$ 15,100). The nmr spectrum showed maxima for 2 olefinic protons as a singlet at 5.9 (4 position) and as a multiplet between 5.28 and 5.48 (7 position), 2 allylic protons as a multiplet between 2.8 and 3.7 ppm (6 position), and 3 protons as a singlet at 0.80 ppm (18 position). Its infrared spectrum was identical with that of an authentic sample.

(1) H. J. Ringold and S. K. Malhotra, *Tetrahedron Lett.*, No. 15, 669 (1962).

(2) E. L. Shapiro, T. Legatt, L. Weber, and E. P. Olivetto, *Steroids*, **3**:2, 183 (1964).

(3) R. Antonucci, S. Bernstein, R. Littell, K. J. Sax, and K. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952).

(4) J. A. Zderic, H. Carpio, A. Bowers, and C. Djerassi, *Steroids*, **1**, 233 (1963).

(5) Melting points were determined with a Thomas–Hoover apparatus and are corrected. Ir spectra were determined with a Perkin-Elmer spectrophotometer, Model 21; nmr spectra were determined in deuteriochloroform with a Varian A-60 spectrometer; and chemical shifts are reported in parts per million downfield from tetramethylsilane.

(6) Productos Esteroides, Naucalpan, Mexico.