A 19-mg sample of the aldehyde was cyclized with acid and the product crystallized twice from methanol to yield 9 mg (53%) of yellow crystals, mp 131.5–137.5°. Further recrystallization (four times) produced material of mp 138–142°.

Registry No.—Tazettine, 507-79-9; dihydrotazettine methine alcohol, 16831-67-7; (−)-(*S*)-β-methoxyadipic acid dimethyl ester, 16859-76-0; dieuteriotazettine, 16831-30-4.

The Perchloric Acid Catalyzed Acetic Anhydride Enol Acetylation of Steroidal Δ4-3 Ketones

A. J. LISTON[1] AND P. TOFT

Research Laboratories, Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Canada

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The perchloric acid catalyzed acetic anhydride acylation of 17β-hydroxyandrost-4-en-3-one gave complex mixtures of products in which both O and C acylation occurred. The major constituents of the reaction were 3,17β-diacetoxy-2-acetylandrosta-2,4-diene (6) and 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (3).

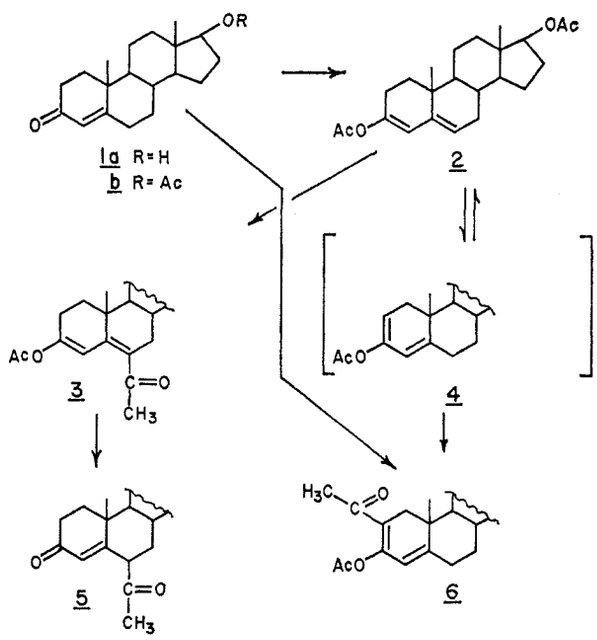
It was previously demonstrated that the C-11β-hydroxyl group of steroids has a pronounced influence on the enolization properties of 3-oxo-5β steroids as measured by the thermodynamically controlled enol acetylation reaction which employs acetic anhydride–perchloric acid mixtures.[2] In order to measure this effect in the biologically active steroids, it became necessary to investigate the perchloric acid–acetic anhydride enol acetylation of Δ4-3 ketones. There are reports[3–6] that this mixture is capable of carrying out O acylations on unsaturated compounds; however, the reagent has not been carefully studied with Δ4-3 ketones.

17β-Hydroxyandrost-4-en-3-one (**1a**) was treated with a solution of perchloric acid in acetic anhydride and the reaction was quenched in 40 min. Gas chromatographic analysis (glpc) of the crude reaction mixture indicated the product to be essentially pure 3,17β-diacetoxyandrosta-3,5-diene (**2**). The compound was isolated in 72% yield and identified by comparison with an authentic sample prepared from the isopropenyl acetate enol acetylation of **1a**.[7,8]

When the reaction time of the perchloric acid catalyzed enol acetylation was extended to 4 hr, eight compounds were detected by glpc in the reaction mixture; five were isolated (Scheme I). The first one eluted by preparative glpc was 3,17β-diacetoxyandrosta-3,5-diene (**2**), identified by comparison with authentic material.[7] A second substance, isolated by preparative glpc, was shown to be 17β-acetoxyandrost-4-en-3-one (**1b**) by comparison with known material. Further attempts to isolate the remaining products by preparative glpc were not successful owing to thermal decomposition of the products during chromatography.

Preparative tlc was used to isolate the remainder of the products. From a band at R_f 0.60 there was obtained pure 3,17β-diacetoxy-6-acetylandrosta-3,5-diene which was assigned structure **3** on the basis of its spectral properties. The infrared spectrum demonstrated enol acetate, ester, and conjugated carbonyl bands. The ultraviolet spectrum exhibited absorptions at λ_{max} 281 mμ (ε 7900) and 220 (8800). The predicted absorption maximum by the Scott modification of the Woodward rules[9a] is at 296 mμ. The observed maximum at 281 mμ and the relatively low intensity of the band suggests an extended chromophore with incomplete conjugation due to the *peri* effect from the C-4 vinylic proton.[10,11] The nmr spectrum of 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**) is recorded in Table I and is consistent with the assigned structure. The locations of the angular methyl group signals in the

SCHEME I



(1) To whom enquiries should be made.

(2) A. J. Liston and M. Howarth, *J. Org. Chem.*, **32**, 1034 (1967).

(3) The use of perchloric acid–acetic anhydride acetylating conditions[4] leads to enol–acetate mixtures which reflect the enolization properties of the cyclic ketone.[5] The enol–acetate ratio has been related to the theoretically calculated stability between isomeric enolic forms.[6]

(4) D. H. R. Barton, R. M. Evans, J. C. Hamlet, P. G. Jones, and T. Walker, *J. Chem. Soc.*, 747 (1954).

(5) J. Champagne, H. Favre, D. Vocelle, and I. Zbikowski, *Can. J. Chem.*, **42**, 212 (1964).

(6) A. J. Liston, *J. Org. Chem.*, **31**, 2105 (1966).

(7) The Δ3,5-dienol acetate was conveniently prepared by the isopropenyl acetate method[8] and compared with known material; *cf.* U. Westphal, *Chem. Ber.*, **70**, 2128 (1937).

(8) W. G. Dauben, R. A. Micheli, and J. F. Eastham, *J. Amer. Chem. Soc.*, **74**, 3852 (1952).

(9) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," The Macmillan Co., New York, N. Y., 1964: (a) p 50; (b) p 67.

(10) A similar ultraviolet spectrum for 6-acetylcholesta-3,5-diene with uv absorptions at λ_{max} 281 mμ (ε 6150), 221 (9400), was recorded by Elmes, Hartshorn, and Kirk.[11] In both instances the compounds were strongly levorotatory, the 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**) exhibiting an $[\alpha]^{28}D$ −167.8° and 6-acetylcholesta-3,5-diene having $[\alpha]D$ −159°.

(11) B. C. Elmes, M. P. Hartshorn, and D. N. Kirk, *J. Chem. Soc.*, 2285 (1964).

TABLE I

NMR RESONANCE DATA IN PARTS PER MILLION OF THE POLYACETYLATED REACTION PRODUCTS

Compd	C-18 $-CH_3$	C-19 $-CH_3$	C-3 -OAc	C-17β -OAc	C-2 -Ac	C-6 -Ac	C-4 -H	C-6 -H
1b	0.85	1.20	...	2.03	...	...	5.71 s	...
2	0.83	1.01	2.12	2.03	...	...	5.69 d (J = 2 Hz)	5.38 m
3	0.83	1.08	2.12	2.03	...	2.23	6.29 d (J = 2 Hz)	...
6	0.81	1.14	2.15	2.03	1.90	...	5.71 s	...
8	0.87	1.38	...	2.03	...	...	5.81 s	...

spectra of compounds **2** and **3** are identical indicating the $\Delta^{3,5}$-dienic structure. The presence of a single vinylic proton signal at 6.25 ppm in the spectrum of **3** is consistent with the proposed structure since the conjugated C-6 acetyl group places the C-4 vinylic proton in the deshielding zone of the carbonyl group[12] and is responsible for the shift downfield from the position of the vinylic proton signals in the spectra of compounds **1b** and **2**. The C-4 proton signal is split into a doublet with J = 2 Hz which is indicative of long-range coupling. Similar coupling has been observed by Wiechert and Schulz[13] between the C-4 and C-2 protons of 3,17β-diacetoxy-5α-androsta-1,3-diene.

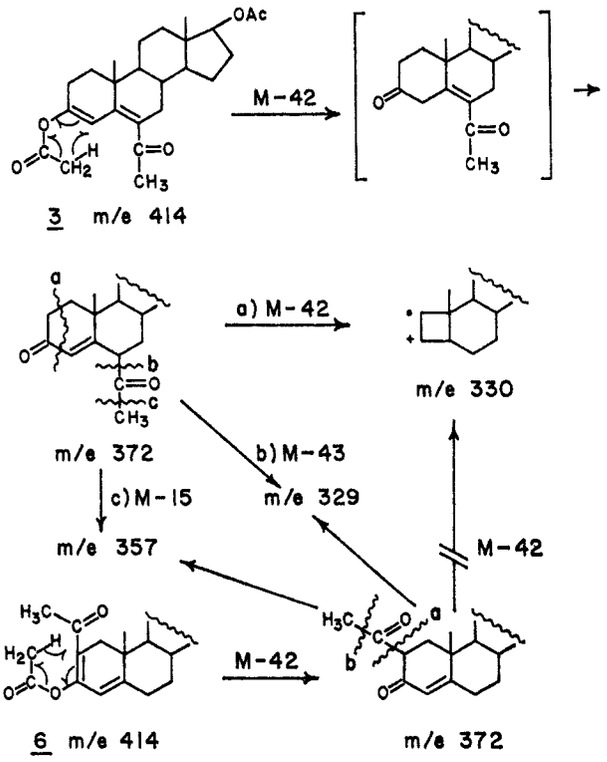
The identity of the compound was further confirmed by treatment with base to saponify the enol acetate function and generate 17β-acetoxy-6β-acetylandrost-4-en-3-one (**5**). The compound was assigned the 6β configuration on the basis of its ultraviolet spectrum, λ_{max} 246 mμ, which is characteristic for the 6β isomer, the epimeric 6α compound has an absorption at λ_{max} 238 mμ.[14] The identity of the saponification product was rigorously established by synthesis of authentic material by the method of Gorodetsky, *et al.*,[14] and comparing the physical properties.[15,16]

The second compound separated from the reaction mixture by preparative tlc was obtained from a band at R_f 0.54. Glpc analysis of the crude material demonstrated two peaks, of which the minor constituent was 17β-acetoxyandrost-4-en-3-one (**1b**) and the major component **6** was the major product of the reaction comprising 45.0% of the total reaction products. Fractional crystallization from acetone–hexane gave pure 3,17β-diacetoxy-2-acetylandrosta-2,4-diene (**6**). The ultraviolet spectrum, λ_{max} 274 (ϵ 9900) and 242 (12,700), is indicative of extended conjugation; however, as with the previous compound **3**, the ultraviolet maximum is lower than the calculated value. This probably reflects the crowding about the C-2 and C-3 positions and the consequent inability to achieve complete conjugation.

The methyl signal of methyl ketones is normally located at δ 2.1 to 2.4 ppm in the nmr spectrum.[17a] However, the C-methyl signal of 3,17β-diacetoxy-2-acetylandrosta-2,4-diene (**6**) is located at δ 1.90 ppm (Table I) which is indicative of a shielding effect by the adjacent O-acetyl group. Examination of molecular models indicates that the crowding about the C-2 and C-3 positions is alleviated by maintaining the C-3 O-acetyl function perpendicular to the plane of the A ring of the steroid. Since the C-2 methyl ketone remains nearly planar because of conjugation it is then situated in the shielding region of the adjacent O-acetyl carbonyl group. The position of the methyl ketone in **6** was verified by saponification of the enol acetate function. The ultraviolet spectrum of the saponification product **7** showed a bathochromic shift in base suggesting a β-diketone structure.

The isomeric dienol diacetates **3** and **6** were subjected to mass spectral analysis and demonstrated similar spectra. Both compounds showed molecular ion peaks at m/e 414. The major fragmentation pattern of 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**) is M^+ 414 → 372 (357, 330, 329). 3,17β-Diacetoxy-2-acetylandrosta-2,4-diene (**6**) gives M^+ 414 → 372 (357, 329). Appropriate metastables were observed in every case. Fragmentation of the enol acetate function in both compounds gives rise to a m/e 372 peak which undergoes fragmentation (*cf.* Scheme II) with loss of either 43 or 15

SCHEME II



mass units. The distinguishing feature which supports the C-2 acetyl assignment in **6** is the absence of a sig-

(12) G. J. Karabatsos, G. C. Sonnichsen, N. Hsi, and D. J. Fenoglio, *J. Amer. Chem. Soc.*, **89**, 5067 (1967).

(13) R. Wiechert and G. Schulz, *Chem. Ber.*, **98**, 3165 (1965).

(14) M. Gorodetsky, E. Levy, R. D. Youssefyeh, and Y. Mazur, *Tetrahedron*, **22**, 2039 (1966).

(15) The hydrolysis product, compound **5**, has the C-6 acetyl group axially oriented, whereas the generally more stable equatorial configuration would be expected. Gorodetsky, *et al.*,[16] have shown that the 17β-acetoxy-6β-acetylandrost-4-en-3-one is more stable than the corresponding 6α epimer. These authors explain this by a possible partial conjugation of the carbonyl group at C-6 with the Δ^4-3-keto group in the 6β-axial compound which is not possible in the 6α-equatorial epimer.

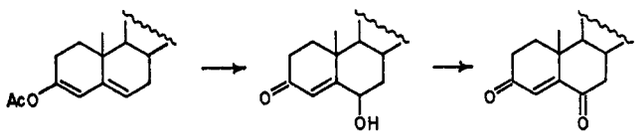
(16) M. Gorodetsky and Y. Mazur, *J. Amer. Chem. Soc.*, **86**, 5213 (1964).

(17) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1966: (a) p 33; (b) p 19.

nificant *m/e* 330 ion[18] whose genesis in **3** is loss of 42 mass units by the well-established loss of ketene from C-2 and C-3 of Δ^4-3 ketones.[19] An unsubstituted C-2 position is required for the latter fragmentation to occur.

A third compound (**8**) separated from the reaction mixture using preparative tlc was isolated in the usual fashion and glpc analysis of the crude material (18 mg) revealed one major product (53%) and four minor constituents. Fractional crystallization yielded pure material which was homogeneous by glpc analysis. The ultraviolet spectrum of the compound demonstrated conjugated carbonyl absorption. Infrared spectroscopy revealed hydroxyl and ester bands and confirmed the presence of a conjugated carbonyl system. The compound was assigned the 17β-acetoxy-6β-hydroxyandrost-4-en-3-one (**8**) structure[20,21] on the basis of its mass spectrum and nmr spectrum. In addition to the signals recorded in Table I there were present two superimposed one-proton multiplets between δ 4.4 and 5.2 ppm. The β configuration of the C-6 hydroxyl group was deduced from additivity constants for the chemical-shift value of the C-19 angular methyl group, which by calculation should be δ 1.39 ppm.[17b] Oxidation of an aliquot of the material with chromium trioxide–pyridine reagent[22] gave a compound whose ultraviolet spectrum was in accordance with the proposed 17β-acetoxyandrost-4-ene-3,6-dione (**9**) structure[9b] (*cf.* Scheme III).

SCHEME III



2 **8** **9**

In previous studies with perchloric acid catalyzed acetic anhydride enol acetylations with saturated keto steroids there was no evidence of C acylation; the O-acylation products were formed almost exclusively.[2,6] Recently Rodig and Zanati[23] investigated the enol acetylation of Δ^1-3-oxo-5α steroids and found at equilibrium some 18% C-acylation product, all of which was formed exclusively at the C-4 position. This would indicate a preferential attack by acetylium ion[24] on the enolic double bond of the diene. Attack on the Δ^1 double bond does not appear to be favored, presumably because of the lack of participation by the enolic acetate function. Rodig and Zanati have speculated that the C acylation could proceed either (a) by direct attack on the α position of the ketone in the enolic form or enol acetate form, or (b) by the Claisen–Haase type of rearrangement involving intramolecular acetyl group migration. Our studies with Δ^4-3 ketones have shown that the first product of the reaction is the $\Delta^{3,5}$-dienol diacetate **2** which is formed almost exclusively using short reaction periods. That compound **2** is the precursor of the C-acylation products was proven by doing parallel experiments with the Δ^4-3 ketone **1** and the dienol diacetate **2**. In both cases glpc analysis of the reaction products after 2 hr demonstrated similar product distributions. In the case of the acetylation of **1** there was detected a 10.5% increase in the formation of 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**) which suggests that a portion of the C-6 acylation is probably formed directly with the major portion of the products being formed by a mechanism involving $\Delta^{3,5}$-dienol diacetate. The product distribution obtained in our studies makes it highly improbable that mechanism b contributes to the reaction, since the rearrangement would lead to C-4-acylated product. It has been possible to account for 97% of the reaction products, none of which was acetylated at C-4.

Attack by acetylium ion on the $\Delta^{3,5}$-dienol diacetate **2** occurred at the C-6 position. Similar results were obtained by Gorodetsky, *et al.*,[14] using boron trifluoride–acetic anhydride mixture. Treatment of 17β-hydroxyandrost-4-en-3-one (**1a**) with this reagent afforded an epimeric mixture of C-6-acetylated 17β-acetoxyandrost-4-en-3-ones (**5**). By extending the reaction period under more forcing conditions they obtained a compound which had undergone C acylation at both C-2 and C-6 positions. The use of perchloric acid as catalyst alters the reaction to produce the enol acetate of compound **5** as a final product. Both methods of acetylation have been postulated as proceeding *via* acetylium ion attack on the enol acetate **2**; however the difference in final products obtained suggests that the Δ^4-3 ketone formed in the boron trifluoride catalyzed acetylation is probably not free but complexed with the reagent and only liberated on working up the reaction mixture. A further variation in the products obtained from the two methods of acylation is the absence of mono-C-acylated product at the C-2 position in the boron trifluoride catalyzed reaction. Using perchloric acid catalyst the major constituent of the reaction was 3,17β-diacetoxy-2-acetylandrosta-2,4-diene (**6**).

The glpc analytical results obtained indicate that there is no appreciable quantity of 3,17β-diacetoxyandrosta-2,4-diene (**4**) present under the equilibrating conditions of the reaction. However, there must be the transient formation of **4** to account for the C-2-acylated product. In cross-conjugated enol acetates, such as **4** or 3,17β-diacetoxy-5α-androsta-1,3-diene,[23] the enolic double bond reacts readily which would explain the high yield of compound **6** in our reaction products. The situation is analogous to that found in the dehydrogenation of Δ^4-3 ketones where it has been suggested that the $\Delta^{2,4}$-dienol is formed by kinetic control and the $\Delta^{3,5}$-dienol by thermodynamic control.[25] The equilibrium point in the presence of acid is almost exclusively on the side of the $\Delta^{3,5}$-dienolic compound.[26] This would signify a rapid attack by acetylium ion on the $\Delta^{2,4}$-dienol acetate **4** which is formed either directly from the Δ^4-3 ketone **1b** or from the equilibration of the $\Delta^{3,5}$-diene **2**.

(18) When the *m/e* 330 peaks in the spectra of **3** and **6** are corrected for the isotope effect from the *m/e* 329 peaks, it can be seen that this peak in the spectrum of **3** corresponds to a major fragmentation route, whereas in **6** it is hardly significant.

(19) R. H. Shapiro and C. Djerassi, *J. Amer. Chem. Soc.*, **86**, 2825 (1964).

(20) 17β-Acetoxy-6β-hydroxyandrost-4-en-3-one has been prepared by oxidizing 3,17β-diacetoxyandrosta-3,5-diene (**2**) with *t*-butyl chromate.[21] The physical properties agree with those of compound **8** isolated herein.

(21) K. Ysuda, *Chem. Pharm. Bull.* (Tokyo), **11**, 1167 (1963).

(22) J. R. Holum, *J. Org. Chem.*, **26**, 4814 (1961).

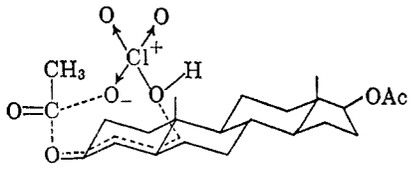
(23) O. R. Rodig and G. Zanati, *ibid.*, **32**, 1423 (1967).

(24) Although the identity of the acetylating species in perchloric acid catalyzed enol acetylations has not been unequivocally established, there is increasing evidence that the acetylium ion must play a significant role in these acetylations. For an excellent review, see D. P. N. Satchell, *Quart. Rev.* (London), **17**, 196 (1963).

(25) A. B. Turner and H. J. Ringold, *J. Chem. Soc.*, 1720 (1967).

(26) H. J. Ringold and K. Malhotra, *J. Amer. Chem. Soc.*, **86**, 1997 (1964).

The isolation of 17β-acetoxy-6β-hydroxyandrost-4-en-3-one is surprising because under strong acetylating conditions the 6β-hydroxyl group should have undergone almost instantaneous acetylation.[27,28] It is necessary to postulate a complex in which both the Δ^4-3-ketone function and the hydroxyl group are involved. A complex of the type shown below would satisfy these conditions. Decomposition of such a complex during the work-up would liberate compound **8**.



Rodig and Zanati have isolated 3% of 1,17β-diacetoxy-4-methylestra-1,3,5(10)-triene from the enol acetylation of Δ^1-3-oxo-5α steroids.[23] To ascertain that none of the minor unidentified constituents of the reaction mixture was the same rearrangement product, the latter compound was synthesized from 17β-hydroxyandrosta-1,4-dien-3-one by dienone–phenol rearrangement.[29] Glpc analysis of the reaction mixture obtained from the perchloric acid catalyzed enol acetylation with authentic 1,17β-diacetoxy-4-methylestra-1,3,5,(10)-triene demonstrated that the phenolic compound was not formed in the reaction.

In view of the lack of C acylation at tertiary C atoms the enol acetylation of alkyl-Δ^4-3 ketones is being investigated. Such compounds may provide a system in which the equilibrium between $\Delta^{2,4}$- and $\Delta^{3,5}$-dienol acetates may be studied.

Experimental Section

General.—Melting points were determined on an Electrothermal apparatus by the capillary method and are corrected. Rotations were measured in chloroform solution. The infrared spectra were recorded on a Perkin-Elmer Model 221 double-beam spectrophotometer. The ultraviolet spectra were determined in ethanol solution using a Bausch and Lomb Spectronic 502 recording spectrophotometer. The nmr spectra were determined on a Varian A-60A spectrometer in deuteriochloroform and chemical-shift values are given in parts per million (ppm) values measured downfield from tetramethylsilane used as an internal standard. Gas chromatography was carried out on a Model 810 F & M gas chromatograph equipped with dual flame detectors. The columns were 5% Fluoro Silicone FS-1265 (QF-1) on 60–80 mesh Diatoport "S," 8 ft × 4 mm o.d. The carrier gas was helium at a flow rate of 60 cc/min and the column temperature was 230°. Quantitative estimation of mixtures was made by trangulation of the signals. Preparative gas chromatography was carried out on an F & M Model 776 Prepmaster Jr. using 20% QF-1 on 10–60 mesh Diatoport "S" with 8 ft × 1 in. o.d. columns. The carrier gas was nitrogen at a flow rate of 0.8 l./min. The column temperature was 250°. The adsorbant for thin layer chromatography was Merck silica gel G and the solvent was benzene–ethanol (8:1). The mass spectra were carried out on a Hitachi–Perkin-Elmer Model RMU-6D at 50 eV.

3,17β-Diacetoxyandrosta-3,5-diene (2).—17β-Hydroxyandrost-4-en-3-one (**1a**, 4.5 g) was suspended in isopropenyl acetate (100 ml) and concentrated sulfuric acid (0.08 ml) was added. The mixture was refluxed for 1.5 hr and the solvent was then partially distilled under reduced pressure. After cooling, the residue was diluted with ether (100 ml) and extracted with 5% aqueous sodium bicarbonate (100 ml). The ether layer was washed with salt solution and dried (Na_2SO_4), and the solvent was evaporated to dryness. The residue (6.1 g) was crystallized from ether to give 3,17β-diacetoxyandrosta-3,5-diene (2.58 g), mp 143–147° (lit.[7] mp 149–150°).

The Reaction of 17β-Hydroxyandrost-4-en-3-one with Perchloric Acid–Acetic Anhydride Reagent.—To a solution of 17β-hydroxyandrost-4-en-3-one (**1a**, 1 g) in carbon tetrachloride (40 ml) and benzene (100 ml) was added a solution (10 ml) of acetic anhydride–70% perchloric acid (49:1). The mixture was stirred at room temperature for 40 min and the reaction was quenched by pouring it into sodium bicarbonate solution (150 ml). The organic material was extracted with two 150-ml portions of ether and the ether solution was dried (Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residual oil was analyzed by glpc. The product consisted of 3,17β-diacetoxyandrosta-3,5-diene (**2**, 72%) and 17β-acetoxyandrost-4-en-3-one (**1b**, 24%). The mixture was separated by preparative glpc. The first product collected was 3,17β-diacetoxyandrosta-3,5-diene (**2**, 700 mg), mp 145–146°; the mixture melting point determination with authentic material previously prepared showed no depression. The second compound isolated by preparative glpc was 17β-acetoxyandrost-4-en-3-one (**1b**, 300 mg), mp 141–143°; the mixture melting point with authentic material was undepressed.

In a similar reaction using 17β-hydroxyandrost-4-en-3-one (**1a**, 1 g) the reaction period was extended to 4 hr and the reaction was quenched as previously described. The crude product was analyzed by glpc and eight compounds were detected: at retention time 8.8 min, 6.3% 3,17β-diacetoxyandrosta-3,5-diene (**2**); at retention time 16.3 min, 10.2% 17β-acetoxyandrost-4-en-3-one (**1b**); at retention time 20.0 min, 0.6% unidentified product; at retention time 23.5 min, 0.2% unidentified product; at retention time 25.3 min, 0.4% unidentified product; at retention time 28.3 min, 4.5% 6β-hydroxyandrost-4-en-3-one (**8**); at retention time 38.8 min, 30.8% 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**); and, at retention time 42.4 min, 45.0% 3,17β-diacetoxy-2-acetylandrosta-2,4-diene (**6**).

The crude material was separated by preparative tlc using a 500-μ layer of silica gel and solvent system benzene–ethanol 19:1. The mixture was deposited (70 mg/20-cm-square plate) from methylene chloride solution as a 5-mm-wide band. The bands were detected by ultraviolet light (R_f 0.54, 0.57, 0.60, and 0.75) and aspirated from the plates. The products were eluted from the adsorbant by washing with acetone and filtering.

From the band at R_f 0.60 there was isolated an oil (100 mg) which was homogeneous by glpc analysis (retention time 38.8 min). Crystallization from acetone–hexane gave pure 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**, 88 mg): mp 140–141°; $[\alpha]^{28}D$ −168° (*c* 0.5); uv max, 281 mμ (ε 7900), 220 (8800); ir (CCl_4), 1758 (>C=C(–OCOCH₃)–), 1735 (–OCOCH₃), 1685 (>C=O), and 1657 cm^{-1} (>C=C<); the nmr spectrum is recorded in Table I; mass spectrum, *m/e* (relative intensity) 414 (5), 373 (26), 372 (100), 357 (15), 330 (18), and 329 (23).

Anal.[30] Calcd for $C_{25}H_{34}O_5$: C, 72.43; H, 8.27. Found: C, 72.72; H, 8.43.

From the band at R_f 0.54 there was obtained an oil (70 mg) which was demonstrated by glpc analysis to consist of 17β-acetoxyandrost-4-en-3-one (**1b**, 26%), retention time 16.3 min, and 3,17β-diacetoxy-2-acetylandrosta-2,4-diene (**6**, 74%), retention time 42.4 min. Fractional crystallization from acetone–hexane gave pure 3,17β-diacetoxy-2-acetylandrosta-2,4-diene (**6**, 11 mg): mp 158–159°; $[\alpha]^{28}D$ 102° (*c* 0.5); uv max, 274 mμ (ε 9900), 242 (12,700); ir (KBr), 1759 (>C=C(–OCOCH₃)–), 1730 (–OCOCH₃), 1675 (>C=O), and 1653 cm^{-1} (>C=C<); the nmr spectrum is recorded in Table I; mass spectrum, *m/e* (relative intensity) 414 (3), 373 (26), 372 (100), 357 (14), 330 (7), and 329 (25).

Anal. Calcd for $C_{25}H_{34}O_5$: C, 72.43; H, 8.27. Found: C, 72.45; H, 8.25.

From the band at R_f 0.75 there was obtained an oil (18 mg) which by glpc analysis was shown to consist of five compounds, the major constituent (53%, retention time 28.3 min) was 17β-acetoxy-6β-hydroxyandrost-4-en-3-one (**8**). The mixture also contained 20% 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**), retention time 38.8 min. The mixture was crystallized from acetone–hexane and there was obtained homogeneous (glpc)

(27) Recently it has been shown that steroidal $\Delta^{3,5}$-dienol ethers are autoxidized to give 6-hydroxy-Δ^4-3 ketones[28] by a free-radical process. Obviously such a mechanism is not operating under our strong acidic conditions since no 3,6,17β-triacetoxyandrosta-3,5-diene was detected.

(28) R. Gardi and A. Lusignani, *J. Org. Chem.*, **32**, 2647 (1967).

(29) C. Djerassi, "Steroid Reactions," Holden-Day, Inc., San Francisco, Calif., 1963, p 371.

(30) Microanalyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y.

17β-acetoxy-6β-hydroxyandrost-4-en-3-one (**8**) (4 mg): mp 202–203.5°; uv max, 237 mμ (ε 19,600); ir (KBr), 3460 (–OH), 1730 (–$OCOCH_3$), 1668 (>C=O), and 1615 cm^{-1} (>C=C<); the nmr spectrum is recorded in Table I; the mass spectrum had a molecular ion peak at *m/e* 346.

The Oxidation of 17β-acetoxy-6β-hydroxyandrost-4-en-3-one (8).—A solution of 17β-acetoxy-6β-hydroxyandrost-4-en-3-one (**8**, 2 mg) in pyridine (0.5 ml) was added to a stirred suspension of chromium trioxide (67 mg) in pyridine (6 ml). The mixture was stirred for 17 hr and poured into sodium bicarbonate solution (25 ml) and extracted with ether (20 ml). The ether extract was washed with 3 *N* sulfuric acid (20 ml), saturated bicarbonate solution (20 ml), and salt solution until neutral. The ether solution was dried (Na_2SO_4) and filtered, and the solvent was evaporated to dryness. Glpc analysis of the product gave a single peak at retention time 29.6 min. The material failed to crystallize but demonstrated the spectral properties consistent with 17β-acetoxyandrost-4-ene-3,6-dione (**9**): uv max, 250 mμ (ε 17,000); ir (CCl_4), 1740 (–$OCOCH_3$), 1710 (>C=O), and 1690 cm^{-1} (>C=O). The product (1.5 mg) was partitioned between 5% sodium hydroxide (5 ml) and ether (5 ml). Glpc analysis indicated the retention of the product in the ether layer.

17β-Acetoxy-6β-acetylandrost-4-en-3-one (5).—A solution of 3,17β-diacetoxyandrosta-3,5-diene (**2**, 1.37 g) in acetic anhydride (20 ml) was treated with boron trifluoride etherate (4.1 ml) at 25° for 4 min, then poured into ice water (200 ml). The aqueous suspension was extracted with ether (100 ml), and the ether solution was washed with sodium bicarbonate solution (100 ml) and then with brine until neutral. The ether solution was dried ($MgSO_4$) and filtered, and the solvent was concentrated under reduced pressure. After cooling, the material was filtered and there was obtained 17β-acetoxy-6β-acetylandrost-4-en-3-one (**5**, 400 mg): mp 162–164°; uv max, 246 mμ (ε 12,000) [lit.[14] mp 165–166°; uv max, 246 mμ (ε 13,000)].

Saponification of Compounds 3 and 6. A.—To a solution of 3,17β-diacetoxy-6-acetylandrosta-3,5-diene (**3**, 20 mg) in methanol (5 ml) was added a saturated solution of sodium acetate (1 ml). The solution was refluxed for 3 hr, and the solvent was removed *in vacuo*. The residue was partitioned between ether (20 ml) and water (20 ml), the organic layer was dried (Na_2SO_4) and filtered, and the solvent was concentrated to dryness. Crystallization from acetone–hexane gave 17β-acetoxy-6β-acetylandrost-4-en-3-one (**5**, 6 mg): mp 151–155°, uv max, 246 mμ (ε 11,900); ir (KBr), 1735 (–$OCOCH_3$), 1712 (>C=O), 1678 (>C=C–C=O), and 1608 cm^{-1} (>C=C<). The ir spectrum was identical with that of an authentic sample. Admixture with authentic material gave a single tlc spot at R_f 0.86 and the mixture melting point was undepressed.

B.—Compound **6** (1 mg) was treated as above. The saponification product **7** had uv max 241 mμ; addition of 5% potassium hydroxide solution caused a bathochromic shift to 425 mμ. Insufficient material was available to characterize the compound further.

1,17β-Diacetoxy-4-methylestra-1,3,5(10)-triene.—To a solution of 17β-hydroxyandrosta-1,4-dien-3-one (1.0 g, mp 167–169°) in carbon tetrachloride (40 ml) and benzene (100 ml) was added a solution of acetic anhydride–70% perchloric acid (10 ml, 49:1). The mixture was stirred at room temperature for 2.5 hr after which the reaction mixture was diluted with ether (100 ml) and washed with two 150-ml portions of sodium bicarbonate solution. The ether layer was washed until neutral with brine and dried (Na_2SO_4). The solution was filtered and the solvent was removed under reduced pressure. Two crystallizations from acetone–hexane gave 1,17β-diacetoxy-4-methylestra-1,3,5(10)-triene (840 mg): mp 139–140° (lit.[31] mp 138.5–139°); uv max, 278 mμ (ε 257); ir (CCl_4), 1759 (>C=C–$OCOCH_3$) and 1740 cm^{-1} (–$OCOCH_3$).

An aliquot of the material was added to the reaction mixture consisting of **2** treated with acetic anhydride–perchloric acid reagent and a new peak was detected by glpc analysis at retention time 8.2 min.

Registry No.—Perchloric acid, 7601-90-3; acetic anhydride, 108-24-7; **1b**, 1045-69-8; **2**, 1778-93-4; **3**, 16853-04-6; **6**, 16803-41-1; **8**, 13096-48-5.

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(31) (a) A. L. Wilds and C. Djerassi, *J. Amer. Chem. Soc.*, **68**, 2125 (1946); (b) C. Djerassi, G. Rosenkranz, J. Romo, J. Pataki, and St. Kaufmann, *ibid.*, **72**, 4540 (1950).

Steroidal C-17 Allene Acetates and Their 17(20)-Unsaturated C-21 Aldehyde Derivatives

WALTER R. BENN

Division of Chemical Research, G. D. Searle & Co., Chicago, Illinois 60680

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A number of examples of steroid derivatives bearing an acetoxyallene side chain at C-17 have been synthesized. In the case of the 3-acetoxy-5-ene derivatives, both isomeric allenes **2a** and **3a** were isolated and the stereochemistry was established by their unique spectral properties. Hydrolysis of the allenic esters lead to conjugated C-21 aldehydes in high over-all yields.

The allenic structure has proven to be a most intriguing system to the chemist from the standpoint of theoretical interest as well as synthetic challenge. The great span of time from van't Hoff's early prediction of the existence of asymmetry in the system to the successful demonstration of this fact stemmed from the lack of good synthetic methods of preparation and resolution. The past several years has seen the development of new routes of stereospecific syntheses of allenes. These are enumerated in the recent review of allene chemistry by Taylor.[1]

Noting the absence of examples of steroidal allenes, some years ago we embarked on a program directed toward the incorporation of this rather novel system into a representative group of steroids.[2] In this first paper we will describe the preparation of a series of steroidal allenic esters and some of the unsaturated aldehydes derived therefrom. The products under consideration are isomeric with, and in fact derived from, a class of compounds of considerable physiolog-

(1) (a) D. W. Taylor, *Chem. Rev.*, **67**, 317 (1967). (b) *Cf.* also the section on cumulenes in H. Fischer, "The Chemistry of Alkenes," S. Patai, Ed., Interscience Publishers, Inc., London, 1964, p 1025.

(2) Since this work has initiated, two papers have appeared describing examples of steroidal allenes: (a) R. Vitali and R. Gardi [*Gazz. Chim. Ital.*, **96**, 1125, 3203 (1966)] have employed the Claisen rearrangement of propargylic enol ethers to introduce the three carbon allenyl group adjacent to a carbonyl function; (b) *cf.* also N. K. Chaudhuri and M. Gut, *J. Amer. Chem. Soc.*, **87**, 3737 (1965).