whose assistance and advice are gratefully acknowledged. The authors are also grateful to Dr. H. Agahigian, W. W. Harple, H. G. Nadeau, Dr. R. Rittner, and their co-workers for performing instrumental and microanalytical work, and for analysis of the infrared and nuclear magnetic resonance spectra.

The Dehydrobromination of 3-Methoxy-17α-bromoestra-1,3,5(10)-trien-16-one

WILLIAM F. JOHNS

Division of Chemical Research, G. D. Searle and Company, Chicago 80, Illinois

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The title reaction is effected with a variety of reagents, leading in part to the formation of 3-methoxyestra-1,3,5(10),14-tetraen-16-one.

Although two different synthetic routes to the C-17α bromides of 16-ketoandrostanes[1] and estratrienes[2] have been described in the literature, few of the reactions of these compounds have been described. To explore the chemical reactivity of this α-halo ketone system as well as the biological activity of resulting products, several transformations of the 17-bromo ketone **1a** were investigated.

One of the initial phases of this problem involved production of 17β-halo steroids by displacement reactions. Accordingly, the bromo ketone **1a** was treated with lithium chloride in dimethylformamide. To effect complete reaction, as measured by the absence of bromine in the product, extended treatment at 100° was necessary. This can be contrasted to the analogous displacement in the 16α-bromo ketone **10** in which case the reaction is complete within a few hours at room temperature.[2] This large difference in reaction rates affords a measure of the relative steric accessibility of the bromine atoms in these two electronically similar systems.

The major product, isolable by direct crystallization, was an unsaturated ketone, $C_{19}H_{22}O_2$, (λ_{max} 5.89 μ and λ_{max} 231 mμ), initially assigned the structure **3**. This product was thought to have been formed by the elimination of the C-17α bromine atom with a simultaneous retropinacolic rearrangement. Due to the *trans* diaxial arrangement of the bromine atom and carbon atoms 13, 17, and 18, this reaction would be expected to occur with fair ease.[3,4] That the assigned structure was incorrect became clear on inspection of its n.m.r. spectrum: the absorption of the methyl group, although shifted, showed that the group was still tertiary and not attached to a carbon–carbon double bond; further, a single vinyl proton showed clearly. The structure 2 was then postulated as best fitting this data. Additional evidence for this structure was obtained by hydrogenation of the unsaturated ketone, a reaction which occurred rapidly. The product, the cyclopentanone **5** (λ_{max} 5.75 μ), showed a molecular rotatory dispersion curve typical of *cis*-hydrindanones; its n.m.r. spectrum was seen to have a tertiary methyl group (72 c.p.s.), but no vinyl proton. A preliminary infrared comparison indicated the unsaturated ketone **2** to correspond to the racemic isomer B of this structure prepared by Wilds and Doban by total synthesis.[5] A more complete infrared comparison of the saturated ketone **5** with their racemic *trans–syn–cis* isomer of that structure confirmed the identity.

A second compound obtained from the lithium chloride reaction was isolated after chromatography. Its analysis and spectrum showed clearly that it was the 17β-chloro ketone **4b**. A comparison with a sample prepared by epimerization[2] of the 17α-chloro ketone **1b** proved the structure of this product.

The unsaturated ketone **2** had also been isolated in earlier epimerization studies of the 17α-bromo ketone **1a**. The acid-catalyzed epimerization of this compound is a very slow reaction, successful conversion requiring prolonged treatment in boiling acetic acid containing toluenesulfonic acid.[2] When ethanolic sulfuric acid was used, an anomalous change in the rotation was seen. Instead of the levorotatory shift expected of the 17α to β isomerization, a marked dextrorotatory change was observed. Analysis of the product by chromatography showed that this phenomenon was due to the competitive formation of ketone **2**, a process precluding measurement of the 17α–β equilibrium ratio here. It is interesting to note that no dehydrohalogenation (to yield ketone **2**) was seen when toluenesulfonic acid–acetic acid was used.

Further work was undertaken to define better the conditions necessary to produce ketone **2** and also to determine the feasibility of producing ketone **3**. To this end a more normal type of elimination reaction was tried, that using collidine. Again the reaction of the 17α-bromo ketone **1a** required much more vigorous conditions than did the 16-bromo-17-ketoandrostane.[6] The product from a sixteen-hour reflux in collidine contained both 17α- and 17β-bromo ketones (**1a**, **4a**) as well as the unsaturated ketone **2**. After the reaction had proceeded for forty hours, no 17α-bromo compound remained. The major product was the unsaturated ketone **2**. Also found were smaller amounts of the 17β-bromo ketone **4a** and the reduction product, 3-methoxyestratrien-16-one (C-14α isomer of **5**). No trace of the isomer **3** was seen despite careful chromatographic inspection.

The reaction of the 17α-bromide with sodium methoxide was expected *a priori* to effect epimerization of the bromide[1,2] and, secondly, to produce the hydroxy ketal

(1) (a) J. Fajkos and J. Joska, *Collection Czech. Chem. Commun.*, **26**, 1118 (1961); (b) J. Fajkos, J. Joska, and F. Sorm, *ibid.*, **27**, 64 (1962); (c) J. Fishman, *J. Org. Chem.*, **27**, 1745 (1962).

(2) G. P. Mueller and W. F. Johns, *ibid.*, **26**, 2405 (1961).

(3) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).

(4) See W. F. Johns, *J. Org. Chem.*, **26**, 4583 (1961), for references to and the description of similar rearrangements in the steroidal D-ring.

(5) We wish to thank Prof. Alfred Wilds for making possible this comparison; see Robert C. Doban, Ph.D. thesis, University of Wisconsin, 1952; A. L. Wilds and T. L. Johnson, *J. Am. Chem. Soc.*, **70**, 1166 (1948); Donald W. Stoutamire, Ph.D. thesis, University of Wisconsin, 1957.

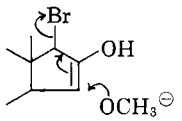
(6) R. Pappo, B. M. Bloom, and W. S. Johnson, *J. Am. Chem. Soc.*, **78**, 6347 (1956).

9.[2] The first of these possibilities was realized by slurrying the α-bromo ketone **1a** in methanolic sodium methoxide, causing a rapid change in crystal form. Filtration of the reaction mixture afforded in good yield the 17β-isomer **4a**. The same procedure on the 17α-chloro compound **1b** similarly effected ready epimerization.[7]

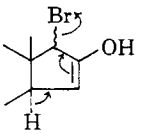
The second product anticipated, the hydroxy ketal **9**, is a normal by-product of the Favorskiĭ reaction.[8] The analogous compound **11** was formed in excellent yields from the 16α-bromo ketone **10**[2] and it was of interest to see if this reaction path would again be favored over the other possibilities available. Using sodium methoxide in a homogeneous reaction effected quick elimination of halogen and afforded a number of products. (The same products were also obtained by prolonged treatment with potassium carbonate in aqueous methanol at room temperature.) The unsaturated ketone **2** was readily isolated and identified by chromatography. Also isolated were two methoxy ketones, easily recognized by their n.m.r. spectra and elemental analyses. One of these was identified by comparison to the known 3,17α-dimethoxyestratrien-16-one (**6**),[9] presumably formed by direct displacement of the C-17β bromide with methoxide ion.

The second methoxy ketone (**7**) was shown to be epimerized by base to another methoxy ketone (**8**), also isolable in small amounts from the original reaction mixture. This interconversion led to an equilibrium consisting approximately of 60% of **8** and 40% of **7**. Assignment of structures to this pair was made possible by observing their clear physical and spectral dissimilarity to any of the known 17-methoxy-16-ketones or 16-methoxy-17-ketones.[9] Deep-seated rearrangements are unlikely because of the normal n.m.r. signal for the angular methyl group. Thus, by elimination there remains only the structures **7** and **8** for this epimeric pair.

Introduction of the 15-methoxyl can be postulated as occurring by an S_N2' reaction,[10] involving the intermediate **i**. Configurational assignments cannot be



i

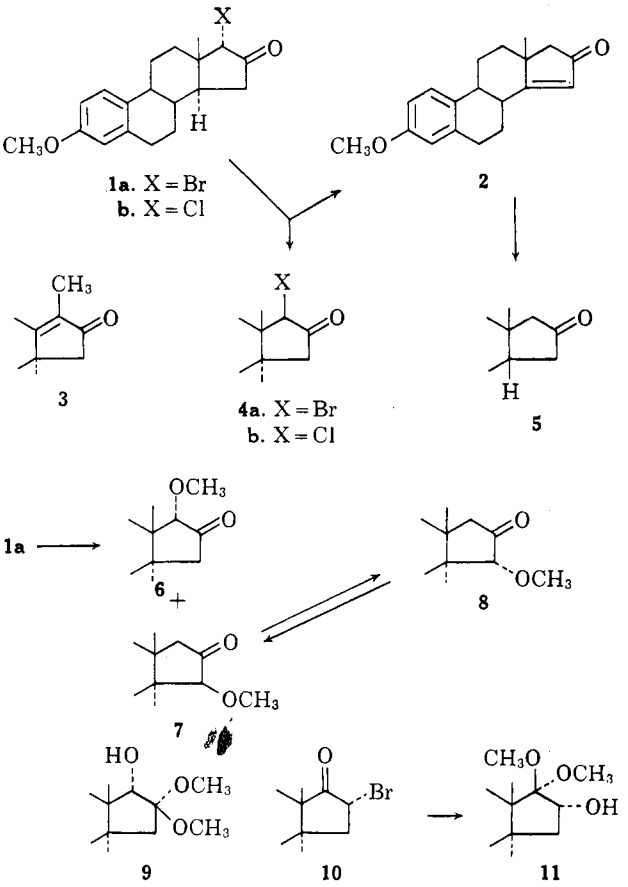


ii

made from mechanistic considerations, since it is possible that the C-17 bromine may be in either configuration before the displacement occurs. The n.m.r. spectra also presents a confused picture of the methoxyl configurations. Tentative assignments are made on the basis of the preponderance of the epimer **8** at equilibrium and also on the shift observed in the infrared: the pseudo-equatorial isomer (**8**) exhibits a maximum at a slightly lower wave length than the β-methoxy ketone **7**.[10b]

This type of dehydrohalogenation previously has been described in the literature, most typically in the case of 2-bromo-3-keto steroids (although in low yield)[11] and in similarly substituted decalins.[12] The simplest mechanistic path for the reaction would be a vinylogous elimination (through the intermediate **ii**).[13] Other mechanisms involving initial carbonium ion formation at C-17 followed by a hydride ion shift, or alternatively, passage through a Favorskiĭ rearrangement intermediate[14] can be envisioned, but are less likely. Isomerization to the C-17 bromine to C-15 during the acid-catalyzed elimination is also improbable.[15]

In simpler steroids the C-17α hydroxyl or halide is readily eliminated with simultaneous angular methyl



migration in contrast to the much more stable C-17β substituted molecules. In the present case, since the 17α halide exists in a definite equilibrium concentration with its epimer, a similar rearrangement would be expected. That this reaction does not occur can be attributed to the presence of the adjacent carbonyl group. Although the carbonyl group is not normally thought of as hindering elimination of an adjacent halogen,[16] in this case, at least, such a hindrance does exist,

(7) Fajkos, see ref. 1a, has since reported the use of dilute potassium hydroxide at room temperature as a quick and efficient method for this epimerization in the androstane series.

(8) See A. S. Kende, *Org. Reactions*, **11**, 261 (1960), for a description of this side reaction and leading references.

(9) Four isomeric α-methoxy ketones have been prepared and identified in these laboratories by Dr. Tyner and will be fully described by him in a forthcoming publication. We wish to thank him for his generous cooperation in this area.

(10)(a) J. S. G. Cox, *J. Chem. Soc.*, 4509 (1960); (b) The n.m.r. data given by Y. Kawazoe, *et al.*, *Chem. Pharm. Bull.* (Tokyo), **10**, 338 (1962), for the C-18 methyl signal of epimeric 15-hydroxylated steroids supports the configurations assigned here.

(11) C. Djerassi and C. R. Scholz, *J. Am. Chem. Soc.*, **69**, 2404 (1947).

(12) M. Yanagita and K. Yamakawa, *J. Org. Chem.*, **21**, 500 (1956).

(13) Another even closer example appeared in the literature after completion of this work: W. G. Dauben, G. A. Boswell, and W. H. Templeton, *J. Am. Chem. Soc.*, **83**, 5006 (1961), have described the dehydrobromination of 1-bromo-A-norcholstan-2-one.

(14) H. O. House and W. F. Gilmore, *ibid.*, **83**, 3972 (1961).

(15) *Cf.* C. W. P. Crowne, *et al.*, *J. Chem. Soc.*, 4351 (1956).

(16) See for example the facile dehydrohalogenation of the steroidal A-ring α-bromo ketones by collidine, as in ref. 11.

leaving the indirect reaction, seen here, as the kinetically favored one.

No significant biological activity was found for any of the new compounds described here.

Experimental[17,18]

The Reaction of the 17α-Bromo Ketone 1a with Lithium Chloride.—A solution of 1.60 g. of the bromo ketone **1a**[2] (m.p. 135–137°) in 50 ml. of dimethylformamide containing 3.2 g. of lithium chloride was heated on the steam bath for 40 hr. The solution was cooled and diluted with water. The pale yellow crystals which formed were collected on a filter, washed with water, and dried in a stream of air, yielding 0.40 g. of crystals, m.p. 135–137°. Recrystallization from ether gave 0.13 g. of the analytically pure 3-methoxyestra-1,3,5(10),14-tetraen-16-one (**2**), m.p. 138–140°; $[\alpha]D$ +319°; λ_{max} 5.82 (sh), 5.89, 5.93 (sh) 6.20, 6.33 μ; 75 (C_{18}-CH_3), 350 (C_{15}H) c.p.s.

Anal. Calcd. for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.88; H, 8.05.

The infrared spectrum of this material was very similar to a previously recorded spectrum compound prepared by Wilds and Doban[5]; insufficient compound was available for successive recordings on the same spectrograph. The ultraviolet absorption, λ_{max} 231 (25,000) mμ, was also recorded with an equimolar amount of estrone methyl ether in the reference cell to substract the absorption of the aromatic A-ring from the total absorption, thus showing the maximum of the cyclopentenone system: λ_{max} 234 (19,700) mμ.

The aqueous mother liquors from the reaction were extracted with chloroform and the extract was washed three times with water. Concentration of the dried extract gave 0.9 g. of a stiff foam which was combined with the mother liquors of the crystallization and chromatographed on 80 g. of silica. Elution with 1% ethyl acetate in benzene gave 0.22 g. of material recrystallized from acetone–petroleum ether to yield 0.13 g. of 3-methoxy-17β-chloroestra-1,3,5(10)-trien-16-one (**4b**), m.p. 202–208°. Recrystallization from chloroform–methanol gave rods, melting in part at 205°, resolidifying, and melting at 211–213°. This material was identical to an authentic sample[2] by infrared comparison. Eluted at 5% ethyl acetate in benzene was 0.65 g. of crude unsaturated ketone **2**, recrystallized from acetone–petroleum ether to yield an 0.40 g. of pure **2**, m.p. 137–139° (identity confirmed by infrared comparison).

In an earlier run, using the same concentration of reactants, essentially no reaction was seen after 24 hr. at room temperature. When the solution was heated at 100° for 4 hr., a halogen analysis of the product indicated the mixture to consist of 70% bromo ketone, 10% monochloro ketone, and, by difference, 20% dehydrohalogenated compounds.

Anal. Calcd. for $C_{19}H_{23}BrO_2$: Br, 22.00. Found: Br, 16.14; Cl, 1.20.

3-Methoxy-14β-estra-1,3,5(10)-trien-16-one (5).—A solution of 0.16 g. of the unsaturated ketone **2** in 30 ml. of ethanol containing 0.10 g. of 5% palladium on carbon was stirred in an atmosphere of hydrogen, absorbing one equivalent of gas in 15 min. The solution was filtered and concentrated.[19] The residue was recrystallized from chloroform–methanol yielding 0.13 g. of the ketone **5**, m.p. 155–157°; $[\alpha]D$ +217°; λ_{max}^{KBr} 5.72 μ; 72 (C_{18}-CH_3) c.p.s. This compound was identical in the infrared to the *dl* compound.[5] The rotatory dispersion curve had a positive Cotton effect: λ_{max} 314.5 ([α] +3610°) and 324 (+3160°) mμ; λ_{min} 318 (+3040°) and 284 (−240°) mμ.[20]

Anal. Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.31; H, 8.86.

The mother liquors provided another 15 mg. of **5**; no *trans* isomer was isolated.

Acid-Catalyzed Epimerization of the 17α-Bromo Ketone 1a.—A solution of 1.0 g. of the bromo ketone **1a** in 40 ml. of 95% ethanol and 4 ml. of concentrated sulfuric acid was heated at reflux. After 6 days, the solution was cooled, diluted with water, and extracted with benzene. The extract was washed with aqueous potassium bicarbonate solution, then dried, and concentrated. The residue (0.78 g., $[\alpha]D$ +90°) was chromatographed on 110 g. of silica. (An aliquot of the reaction withdrawn after 2 days and worked up in the same way exhibited $[\alpha]D$ +19°.) Eluted with 0–2% ethyl acetate in benzene was 0.56 g. of semicrystalline material, recrystallized from methylene chloride–methanol twice to give 0.35 g. of the starting material **1a**, m.p. 130–133°. (A paper chromatogram of the mother liquors showed the presence of approximately 10% of the 17β-epimer **4a**.) Elution with 5% ethyl acetate in benzene provided 0.21 g. of residue recrystallized from ether to provide 50 mg. of pure **2**, m.p. 135–137° (identity confirmed by spectral comparison with authentic material.)

Reaction of the 17α-Bromo Ketone 1a with Collidine.—2,4,6-Collidine (30 ml.) containing 1.68 g. of the ketone **1a** was heated at reflux under nitrogen for 42 hr. The solution was cooled, diluted with water and excess 5% hydrochloric acid, and the resulting mixture was extracted with benzene. The extract was washed with aqueous potassium bicarbonate, dried, and concentrated under reduced pressure. The product, 1.15 g. of oil, was chromatographed on 60 g. of silica. Elution with benzene provided 0.10 g. of material, recrystallized from methylene chloride–methanol to yield 80 mg. of the 3-methoxy-17β-bromoestra-1,3,5(10)-trien-16-one (**4a**), m.p. 221–224°, identical in the infrared to an authentic sample.[2] Further elution with benzene gave 0.12 g. of residue, recrystallized from petroleum ether (Darco) to yield 40 mg. of 3-methoxyestra-1,3,5(10)-trien-16-one (**5** with 14α-H), m.p. 122–124°, identical in the infrared to an authentic sample. Eluted with 2% ethyl acetate in benzene was 0.60 g. of material, recrystallized from ether to give 0.46 g. of the unsaturated ketone **2**, m.p. 138–140° (spectral comparison satisfactory).

In an earlier run, after 16 hr. at reflux, the product was chromatographed and shown to consist of 30% of a mixture of 17α- and 17β-bromo ketone fractions. Also present was 40% of the unsaturated ketone **2**.

Reaction of the 17α-Bromo Ketone 1a with Sodium Methoxide. A. Reaction in a Heterogeneous System.—A slurry of 1.0 g. of the bromo ketone **1a** in 40 ml. of methanol containing 3.5 g. of sodium methoxide was stirred at room temperature for 25 min. Although the mixture remained heterogeneous, a definite change in crystal form was seen. The mixture was filtered, the precipitate being washed with methanol and then with water, leaving 0.62 g. of crystals, m.p. 175–215°. Recrystallization from methylene chloride–methanol gave 0.36 g. of the pure 17β-bromide **4a**, m.p. 218–222°, identical to the authentic material by the standard comparisons.

The 17α-chloro ketone (**1b**, 0.10 g.) was similarly epimerized by slurrying in 4 ml. of methanol containing 0.50 g. of sodium methoxide for 10 min. The product, isolated by filtration and purified by recrystallization from aqueous methanol, gave 30 mg. of the pure chloro ketone **4b**, m.p. 196–201°, identical by normal criteria to the authentic material.[2]

In a similar experiment, a solution of 0.10 g. of the chloro ketone **1b** in 6 ml. of methanol and 2 ml. of 5% aqueous potassium hydroxide was allowed to stand at room temperature for 20 min. The product, isolated by benzene extraction, was demonstrated by analysis to have lost halogen.

Anal. Calcd. for $C_{19}H_{23}ClO_2$: Cl, 11.12. Found: Cl, 1.14.

B. Reaction in a Homogeneous System.—To a solution of 9 g. of sodium methoxide in 200 ml. of methanol was added a solution of 1.50 g. of **1a** in 10 ml. of benzene at 5°. A precipitate formed very quickly and remained unchanged despite vigorous stirring and removal of the cooling bath. After 1 hr., the solution was filtered, yielding 0.80 g. of the 17β-bromo ketone **4a**, m.p. 200–215° (infrared comparison). This material (0.78 g.) was dissolved in 80 ml. of benzene and added to the sodium methoxide solution within 30 min. of the filtration. After a total of 5 hr. the homogeneous solution was treated with excess acetic acid and water. The product (1.3 g. of oil) was isolated by benzene extraction and chromatographed on 85 g. of silica.

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(17) We wish to acknowledge the assistance of Dr. E. G. Daskalakis and staff for the chromatographic work and Dr. R. T. Dillon and staff for the analyses and spectra described here.

(18) Melting points were taken on a Fisher-Johns melting point apparatus and are not corrected. Rotations were determined in chloroform (1%), ultraviolet spectra in methanol, and n.m.r. spectra in deuteriochloroform. The n.m.r. spectroscope was Model A-60, Varian Associates, Inc., operating at 60 Mc; the values reported are Δν from tetramethylsilane as an internal standard. The petroleum ether used had b.p. 60–80°.

(19) We wish to thank Mr. W. Selby for conducting this hydrogenation.

(20) We wish to thank Dr. N. L. McNiven for this determination. C. Djerassi, J. Fishman, and T. Nambara, *Experientia*, **12**, 565 (1961), describe the dispersion curves of analogous ketones.

Eluted with benzene and 0.5% ethyl acetate in benzene was 0.62 g. of a crystalline mixture. A paper chromatogram of these fractions showed two components to be present in roughly equal amounts. Partial separation of these compounds was effected by crystallization from methanol and from petroleum ether assisted by mechanical separation, giving rectangular plates, m.p. 126–128°, and prisms, m.p. 158–163°. The lower melting material was seen to be identical to the known 3,17α-dimethoxyestra-1,3,5(10)-trien-16-one (**6**)[9] by comparison of the infrared spectra. The second component was recrystallized from petroleum ether to give the pure 3,15β-dimethoxyestra-1,3,5(10)-trien-16-one (**7**), m.p. 165–168°; $[\alpha]D$ −15°; λ_{max} 5.75 mμ; 63 (C_{18}-CH_3), 210 (15-OCH_3) c.p.s.

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.12; H, 8.50.

Also eluted with 1% ethyl acetate in benzene was 80 mg. of a crystalline mixture recrystallized from petroleum ether and then from methanol to yield 30 mg. of 3,15α-dimethoxyestra-1,3,5(10)-trien-16-one (**8**), m.p. 100–102°; λ_{max} 5.72 mμ; 57 (C_{18}-CH_3), 218 (15-OCH_3) c.p.s.

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 77.09; H, 8.32.

At 5% ethyl acetate in benzene was eluted 0.19 g. of material, recrystallized from acetone–petroleum ether to yield 0.11 g. of the unsaturated ketone, **2**, m.p. 130–135° (spectral comparison satisfactory).

Reaction of the Bromo Ketone 1a with Potassium Carbonate.—To a solution of 0.6 g. of potassium carbonate in 6 ml. of water and 200 ml. of methanol was added 0.30 g. of the bromo ketone **1a**. After 72 hr. the solution was poured into water containing excess acetic acid. The resulting mixture was isolated with benzene in the usual way. The crude product (0.25 g.) was analyzed by paper chromatography and was seen to consist of 40–45% of the 15β-methoxy compound **7**, 35–40% of the 17α-methoxy compound **6** and 3–5% of the 15α-compound **8**. No bromo ketones were seen and less than 5% of the unsaturated ketone **2** was in evidence. Chromatography on silica led to isolation of the two major products as described for the sodium methoxide-catalyzed reaction.

In an earlier experiment, using similar conditions, the reaction was stopped after 18 hr. At that time, analysis of the product by paper chromatography showed 45% of the 17β-bromo ketone **4b**, 20% of the 17α-bromo ketone **1a**, and 15% each of the methoxy ketones **6** and **7**.

Equilibration of the Methoxy Ketones 7 and 8.—A solution of 40 mg. of the methoxy ketone **7** and 0.2 g. of potassium carbonate in 10 ml. of methanol and 2 ml. of water was heated at reflux for 1 hr. The solution was diluted with water and extracted with benzene. Isolation of the product in the usual way afforded 40 mg. of semicrystalline residue. This material was seen by paper chromatography and n.m.r. (methoxyl absorption at 210 and 218 c.p.s.) to consist of about 60% of ketone **8** and 40% of ketone **7**. Attempts at separation by fractional crystallization were only partially successful.

Retreatment of the equilibrium mixture with potassium carbonate in methanol for an additional 2 hr. led to no appreciable change in the proportion of isomers **7** and **8** as seen by paper chromatography.

Acyl Transfer during Chromium Trioxide Oxidation in the Pregnane Series. Some Reactions of 5 β-Androstane-16,17-ketols[1,2]

C. H. KUO, D. TAUB, AND N. L. WENDLER

Merck Sharp and Dohme Research Laboratories, Merck and Company, Inc., Rahway, New Jersey

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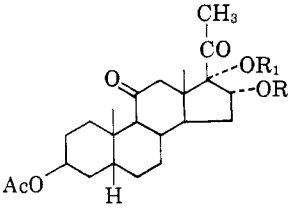
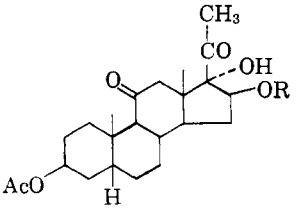
Reaction of 3α,16α-diacetoxy-17α-hydroxypregnane-11,20-dione (Ib) with chromium trioxide in acetic acid proceeded in part anomalously to give the 17α-acetoxy-11,16-20-trione V. The latter compound with base underwent β-ketonic cleavage or rearrangement to give primarily the δ-lactone VIII. Various reactions of the 17β-hydroxy ketol system VIIa are discussed.

In connection with work on the D-homoannulation of the 3α,16-17α-trihydroxy-11, 20-diketopregnanes Ia and IIa,[3] we had occasion to degrade the corresponding 16α- and 16β-acetates, Ib and IIb, to the respective 16-acetoxy 17-ketones by two routes in order to confirm that ring D in the parent compounds was five-membered. In each case, successive treatment with sodium borohydride in aqueous dimethylformamide[4] and sodium metaperiodate[3,5] led to the ketol acetates III and IV, respectively. Both ketol acetates III and IV gave positive blue tetrazolium tests and showed a characteristic shift in the 17-carbonyl infrared band to 5.70 μ from the normal 5.77 μ due to interaction with the 16-acetyl function. This shift was independent of configuration at C-16.[6]



Ia. R = R₁ = H
Ib. R = Ac, R₁ = H
Ic. R = R₁ = Ac



IIa. R = H
IIb. R = Ac

Although the second method of side chain degradation, namely, chromium trioxide in acetic acid, gave analogous results in the 16β-acetoxy series, similar treatment of the 16α-acetate Ib gave a second neutral tetrazolium positive substance (20–25% yield) in addition to the 16α-acetoxy 17-ketone III (30–35%)[7] plus a minor amount of 3α-acetoxy-11-ketoetiobilianic acid (VIb). The infrared spectrum of the new material [λ_{max}^{chf} 5.68, 5.79, 5.84, 8.00 μ] indicated the possible presence of an acetate function adjacent to a carbonyl group as in the ketol acetates III and IV. However, the high negative specific rotation of this substance,

(1) Presented in part before the American Chemical Society, North Jersey Section, Meeting-in-Miniature, February 1, 1960.

(2) In a recent publication entitled, "16-Bromo-D-Homo Steroids," by N. L. Wendler and H. L. Slates [*J. Org. Chem.*, **26**, 4738 (1961)], these authors inadvertently failed to make reference to the reports of C. Djerassi and T. Nakano [*Chem. Ind.* (London), 1385 (1960)] as well as M. Uskoković, M. Gut, and R. I. Dorfman [*J. Am. Chem. Soc.*, **82**, 958 (1960)] bearing on the isomerization and elimination reactions of A and D ring α-halo ketones in related steroid systems. Apologies are herewith expressed for this oversight.—N. L. W.

(3) N. L. Wendler, D. Taub, and C. H. Kuo, *ibid.*, **82**, 5701 (1960).

(4) D. Taub, R. D. Hoffsommer, and N. L. Wendler, *ibid.*, **81**, 3291 (1959).

(5) G. Cooley, B. Ellis, F. Hartley, and V. Petrow, *J. Chem. Soc.*, 4373 (1955), utilized an analogous sodium borohydride-periodate sequence to degrade the side chain in the 3β,16-diacetoxy-5-pregnen-20-one series.

(6) *Cf.* R. N. Jones and G. Roberts, *Chem. Ind.* (London), 1269 (1957).

(7) Cooley, *et al.*, ref. 5, on chromium trioxide oxidation of 3β,16α-diacetoxy-17α-hydroxy-5α-pregnan-20-one observed formation of one neutral product, the expected 16α-acetoxyandrostan-17-one.