Oxidation of Testosterone Acetate with Per Acids

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Received June 16, 1966

Oxidation of testosterone acetate (1) with perbenzoic acid and anhydrous perchloric acid produces the enol lactone (2), the epoxy lactones (3), the aldehydo lactones (4), the 5α-formate (5), and the epoxy ketone (6). The product ratio depends on the quantity of per acid used and on the reaction time. Similar oxidation, with aqueous perchloric acid, leads to the lactone (8) and the A-nor ketone (9). Yet another oxidation product, the lactone acid (17), was isolated when *m*-chloroperbenzoic acid with aqueous perchloric acid was used. The oxidation sequence of testosterone acetate (1), deduced from these results, is discussed.

Per acid oxidation of α,β-unsaturated ketones may, by oxygen insertion between the double bond and the carbonyl group, lead to enol esters, epoxy esters, and epoxy ketones.[1] However, per acid oxidation of Δ^4-3-keto steroids may result in an even larger variety of products, depending on the per acid being used. Thus potassium persulfate and sulfuric acid furnished 3-keto-4-oxa 5α-steroids,[2-5] but perbenzoic acid containing perchloric acid in chloroform was reported to yield a mixture of enol lactones and epoxy lactones.[6] Recently, rearranged products, the 5α-aldehydo-3-keto-4-oxa derivatives, were obtained when Δ^4-3-keto steroids were treated with trifluoroperacetic[7] acid.

We have reinvestigated the oxidation of testosterone acetate (**1**) with perbenzoic acid containing perchloric acid in chloroform solution. Under anhydrous conditions, the following products could be isolated: the enol lactone (**2**), the epoxy lactones (**3**), the aldehydo lactones (**4**), the 5α-formate (**5**), the 4α,5α-epoxy ketone (**6**), and the methyl ester (**7**). (See Scheme I.)

When water was present in the reaction mixture, none of these products was obtained, the main product being instead the saturated lactone (**8**), accompanied by the A-nor ketone (**9**).

Compounds **6**[8] and **9**[9] were identified by comparison with authentic samples, and **8** was transformed into the known corresponding 17β-hydroxy lactone.[10] All other new compounds show infrared spectra, molecular analyses, and mass spectra compatible with the assigned structures. The nmr spectra of these compounds were also in accord with the suggested formulas (Table I).

SCHEME I

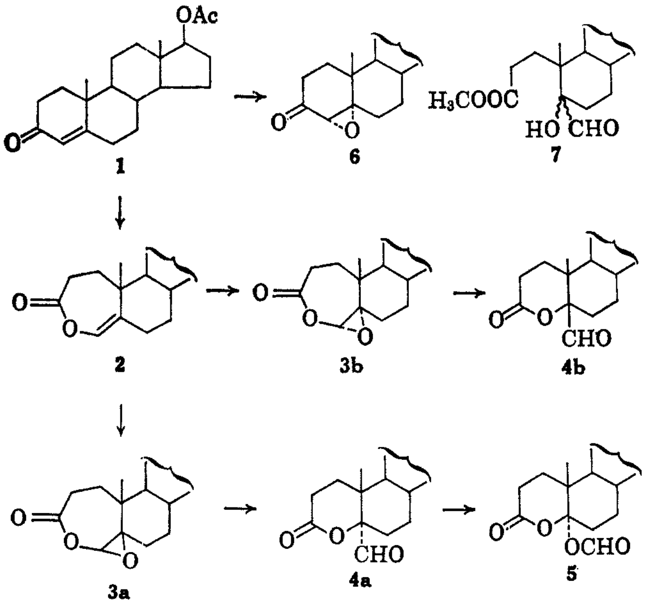

TABLE I

NMR SPECTRA OF OXIDATION PRODUCTS OF TESTOSTERONE ACETATE (1)[a]

Compd	No.	CH$_3$ at C-18	CH$_3$ at C-19	H at C-2[b]	H at C-4′
Enol lactone	**2**	0.81	1.11	2.61	6.05 (CH=C)
Epoxy lactone	**3a**[c]	0.81	1.18	2.60	4.76 ($\mathrm{OCH}\underset{\substack{\Vert \\ \mathrm{O}}}{\mathrm{C}}$)
Epoxy lactone	**3b**[c,d]	0.81	1.18[e]	2.60	4.68 ($\mathrm{OCH}\underset{\substack{\Vert \\ \mathrm{O}}}{\mathrm{C}}$)
Compd	No.	CH$_3$ at C-18	CH$_3$ at C-19	H at C-2[b]	H at C-5
Lactone	**8**	0.81	0.95	2.63	3.88 ($\underset{\substack{\Vert \\ \mathrm{O}}}{\mathrm{C}}\mathrm{OCH}$)
Aldehydo lactone	**4a**	0.84	1.10	2.75	10.10 (CHO)
Aldehydo lactone	**4b**	0.86	1.16	2.55	9.67 (CHO)
Formate	**5**	0.81	1.11	2.70	8.47 (O—CHO)
Carbomethoxy lactone	**10**	0.81	1.08	2.61	3.75 (COOCH$_3$)
Compd	No.	CH$_3$ at C-18	CH$_3$ at C-19	H at C-2[b]	H at C-4
Epoxy ketone	**6**	0.81	1.07	2.35	3.03 (COCHO)
Carbomethoxy-aldehyde	**7**	0.84	1.06		10.2 (CHO)
Carboxy lactone	**17**	0.83	1.33		9.9 (COOH)

[a] The nmr spectra were determined on a Varian A-60 spectrometer. Peak positions are indicated in parts per million downfield from tetramethylsilane serving as internal reference. In some cases the spectra were taken on a 100-Mc Varian spectrometer. [b] Multiplets. [c] Spectrum taken on a 100-Mc Varian instrument. [d] In 1:1 mixture with **3a**. [e] This line was resolved into two peaks at 1.183 and 1.190 ppm.

The structure and stereochemistry of **4a** were established by oxidation of **4a** with Jones reagent, and subsequent methylation with diazomethane. The product **10a** was identical with a compound obtained from **11**[11] by ozonolysis followed by oxidation with Jones reagent. Acid hydrolysis and subsequent oxidation converted

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[1] N. Prilejaeff, *Bull. Soc. Chim. France*, **41**, 687 (1927); J. Boeseken and A. L. Soesman, *Rec. Trav. Chim.*, **52**, 874 (1933); J. Boeseken and Jacobs, *ibid.*, **55** (1936); H. M. Walton, *J. Org. Chem.*, **22**, 1161 (1957); G. B. Payne and P. H. Williams, *ibid.*, **24**, 284 (1959).

[2] A. Salamon, *Z. Physiol. Chem.*, **272**, 61 (1941).

[3] R. B. Turner, *J. Am. Chem. Soc.*, **72**, 579 (1950).

[4] G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, **26**, 986 (1961).

[5] G. R. Pettit and T. R. Kasturi, *ibid.*, **26**, 4557 (1961).

[6] E. Caspi, Y. W. Chang, and R. I. Dorfman, *J. Med. Pharm. Chem.*, **5**, 714 (1962).

[7] J. T. Pinhey and K. Schaffner, *Tetrahedron Letters*, 601 (1965).

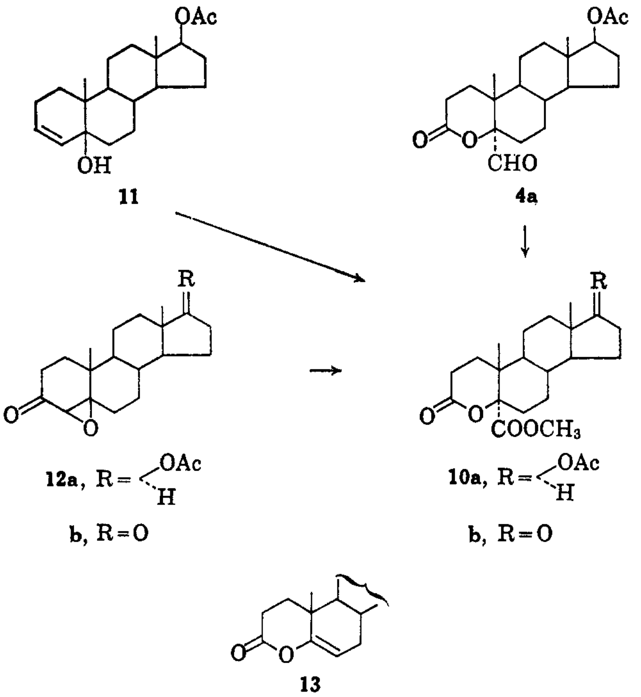
[8] (a) B. Camerino, B. Patelli, and A. Vercellone, *J. Am. Chem. Soc.*, **78**, 3540 (1956); (b) C. Lehmann, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **45**, 1031 (1962).

[9] B. Camerino and V. Valcavi, *Gaz. Chim. Ital.*, **93**, 723 (1963). We are indebted to Dr. Camerino for a sample of this compound.

[10] N. W. Atwater and J. W. Ralls, *J. Am. Chem. Soc.*, **82**, 2011 (1960).

[11] For analogous compound in the cholestane series see P. S. Wharton and D. H. Bohlen, *J. Org. Chem.*, **26**, 3615 (1961).

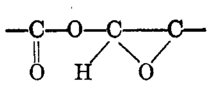
SCHEME II



4a to **10b**, identical with a compound prepared[12] from **12b** by alkaline hydrogen peroxide (Scheme II). This confirms the configuration previously assigned to C-5 in compounds prepared by alkaline peroxidation of 4β,5β-epoxy-3-keto steroids.[13]

The optical rotatory dispersion curve[14] of **4a** (Figure 1) shows two Cotton effects, negative at higher wavelength and positive at lower wavelength. The negative Cotton effect is due to the aldehyde chromophore, while the positive one is probably due to the lactone chromophore, and is of similar shape and magnitude to the one observed in the lactone **8**,[15] of the same stereochemistry at C-5 (Figure 1.)

The structure of **3a** was inferred from its physical properties. Its nmr spectrum[16] shows (Table I) a multiplet owing to two protons α to the lactone carbonyl, as well as a singlet at 4.76 ppm, the latter being assigned to the proton of the



$$-\underset{\substack{\| \\ O}}{C}-O-\underset{H}{C}\underset{O}{\diagdown\!\!\diagup}C-$$

chromophore (Table I). Treatment of **3a** with Lewis acids (dry perchloric acid in chloroform, or boron trifluoride in benzene) effected rearrangement to **4a**, a transformation which occurs also upon heating **3a** above its melting point.

The epoxy lactone **3a** was usually accompanied by crystalline higher melting material whose mass spectrum[17] indicated that it had the same molecular weight as **3a** and a similar fragmentation pattern. Its 60-Mc nmr spectrum was also similar to that of **3a**, but for an additional signal at 4.68 ppm of approximately the same intensity as the one at 4.76 ppm (Table I). Since the integrated area of both nmr signals at 4.68 and 4.76 ppm corresponded to one proton, and the chemical shifts of these two resonances remained unchanged in the 100-Mc spectrum, the 4.68-ppm line could be attributed to epimer **3b** present in a *ca.* 1:1 mixture with **3a**. This mixture of **3a** and **3b**, on treatment with Lewis acid or on heating, isomerized to a 1:1 mixture of two aldehydo lactones one of which was identical with **4a**. To the other aldehyde we assign formula **4b**. In contrast to **4a**, **4b** showed a positive Cotton effect at higher wavelength, and a negative one (superimposed on the previous one) at lower wavelength. The sign of the latter may be indicative of the A/B *cis* stereochemistry in the aldehyde **4b**.

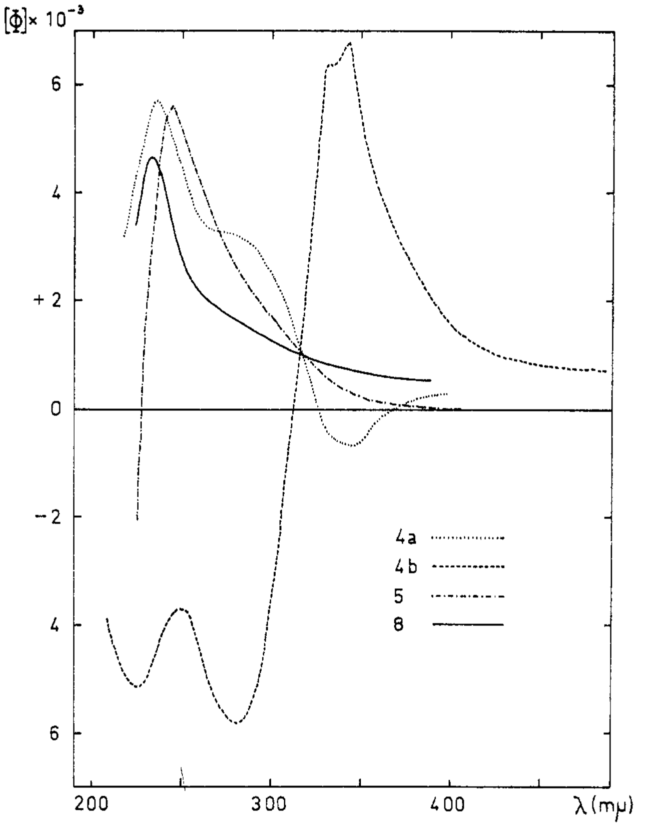


Figure 1.—ORD spectra of 3-keto-4-oxaandrostane derivatives.

The isomerization of the mixture of **3a** and **3b** to the corresponding mixture of the two aldehydo lactones **4a** and **4b** could be followed by nmr spectroscopy. Addition of 1 drop of anhydrous trifluoroacetic acid to the solution of the crystalline mixture of **3a** and **3b** in deuteriochloroform or heating to 120° in deuteriobromoform changes the spectrum instantaneously to that of a 1:1 mixture of **4a** and **4b**.

The facile pyrolytic rearrangement of **3a** and **3b**, indicated by arrows in Chart I, is probably facilitated by proximity of the epoxy oxygen to the carbonyl carbon in these compounds.

The acid-catalyzed rearrangement of **3a** and **3b** may involve protonation of epoxy oxygen followed by cleavage of its bond to C-4′ with subsequent "acyl-O" cleavage of the lactone and formation of an aldehyde and lactone groups.

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(12) G. Hüppi, G. Eggart, S. Iwasaki, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **49**, 1986 (1966). We are greatly indebted to Dr. H. Wehrli, E. T. H. Zurich, for the sample of this compound.

(13) W. Reusch and R. LeMahieu, *J. Am. Chem. Soc.*, **85**, 1669 (1963).

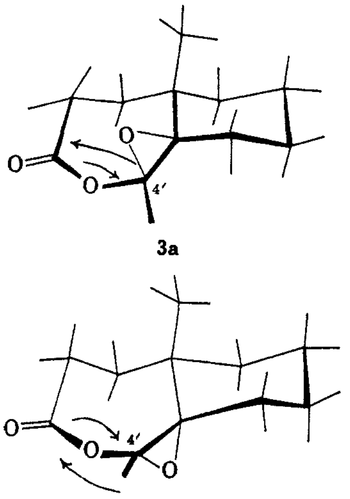
(14) The ORD spectra were determined on a Jasco ORD/UV-5 instrument in cyclohexane solution, using cells of 1-mm width.

(15) For ORD spectra of 3-keto-4-oxa steroids, see H. Wolf, *Tetrahedron Letters*, 1075 (1965).

(16) See Table I, footnote *a*.

(17) Mass spectra were measured with an Atlas CH-4 instrument, samples being introduced directly into the ion source.

CHART I



3a

3b

The structure of **5** is indicated by its transformation to the known **13**[18] on heating to 180° in the solid state. Under 70-ev impact the molecular ion of 5α-formate **5** eliminates a molecule of formic acid so readily that its molecular peak does not appear in the mass spectrum, the highest peak being at (M − 46) *m/e*.

The ORD curve of **5** exhibits a positive Cotton extreme of the lactone chromophore, similar to that observed in lactones **8** and **4a** which have the same *trans* fusion of the A/B rings (Figure 1).

The methyl ester, to which we assign the structure **7**, is probably an artifact, formed by reaction of **3** with methyl benzoate which was invariably present in the chloroform solution of the perbenzoic acid used.

Relative amounts of some of the products obtained in the per acid oxidation of **1** depended on the quantity of perbenzoic acid used and on the duration of the reaction. When **1** was treated with 1 mole equiv of perbenzoic acid for 12 hr, enol lactone **2** (*ca.* 10%)[19] was isolated in addition to about 40% of recovered starting material. With 2 mole equiv of per acid for 12 hr, the major products were epoxy lactones **3** (*ca.* 70%), and aldehydo lactones **4** were found in less than 5%. Reaction of **1** with 2 moles of perbenzoic acid for 84 hr resulted in a higher yield of the aldehydo lactones **4** (*ca.* 15%) and a lower yield of epoxy lactone **3** (*ca.* 40%). When 4 moles of per acid was used in the 84-hr reaction, 5α-formate **5** was isolated in addition to the previously mentioned compounds. 4α,5α-Epoxy ketone **6** (5–10%) was found among the oxidation products in all the experiments and methyl ester **7** in most of them.

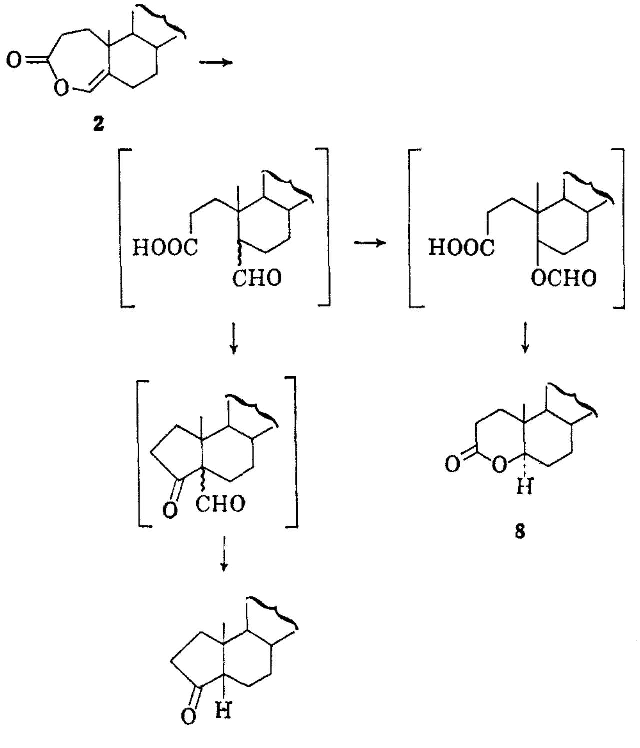
These results indicate a possible sequence for the per acid oxidation of **1**, depicted in Scheme I.

This oxidation sequence is supported by the following observations: **2** reacts with perbenzoic acid, to give mainly epoxy lactones **3**, while **4a** under the same reaction conditions yielded **5**. The only product of the per acid oxidation under anhydrous conditions, which does not fall into this reaction scheme, is 4α,5α-epoxy ketone **6**.

Compound **1** reacted with 2 moles of perbenzoic acid in the presence of *aqueous* perchloric acid to give **8** (30%); the presence of **9** was indicated by thin layer chromatography.

It is reasonable to assume that the primary product of the oxidation of **1** in the presence of water is again enol lactone **2** which may undergo subsequent reaction described by arrows in Scheme III.[20]

SCHEME III



2

8

9

As expected, treatment of **2** with perchloric acid in chloroform containing water, resulted in five-membered ketone **9**. Compound **2** proved to be stable to anhydrous acids, and failed to react with dry perchloric acid in chloroform or with boron trifluoride etherate in benzene.

Compound **1** was also treated with the more reactive *m*-chloroperbenzoic acid in chloroform in the presence of perchloric acid. Under anhydrous conditions, 2 moles of the per acid had already reacted after 12 hr, the main product being **3a** (30%). When the reaction mixture was left under the same conditions for a longer time, most of epoxy lactone **3a** isomerized to **4a**, the main product isolated.

Finally, oxidation of **1** was performed with 2.1 moles *m*-chloroperbenzoic acid in chloroform containing *aqueous* perchloric acid. As in the analogous perbenzoic acid oxidation, both **8** and **9** were isolated. In addition to these, however, the aldehydo lactone **4a** and a new acid were found. The molecular weight of this acid (by mass spectrometry) and the comparatively low-field nmr signal of the C-19 methyl group (Table I) point to structure **14**.[21]

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[18] G. I. Fujimoto, *J. Am. Chem. Soc.*, **73**, 1856 (1951).

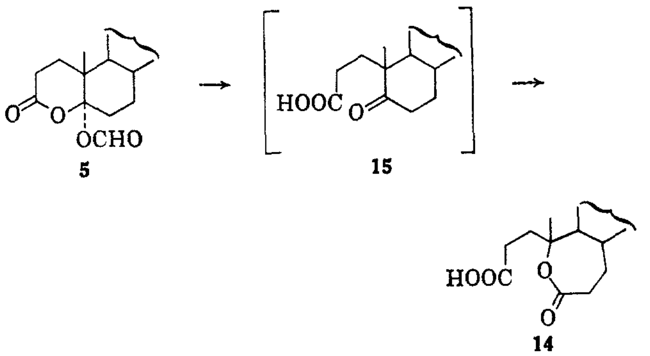
[19] The yields were calculated from the nmr spectra of the total material. The yields of the isolated products are given in the Experimental Section.

[20] The alternative formation of the A-nor ketone **9** from 4,5-epoxy 3-ketones [*cf.* D. J. Collins, *J. Chem. Soc.*, 3919 (1959)] seems to be less likely.

[21] An analogous compound, a 17β-propionate, has been obtained by exhaustive peroxidation of testosterone propionate with an aqueous solution of hydrogen peroxide in *t*-butyl alcohol containing selenium dioxide. This oxidation of Δ^4-3-keto steroids involves probably an analogous sequence as the per acid oxidation: E. Caspi and S. N. Balasubrahmanyam, *J. Org. Chem.*, **28**, 3383 (1963).

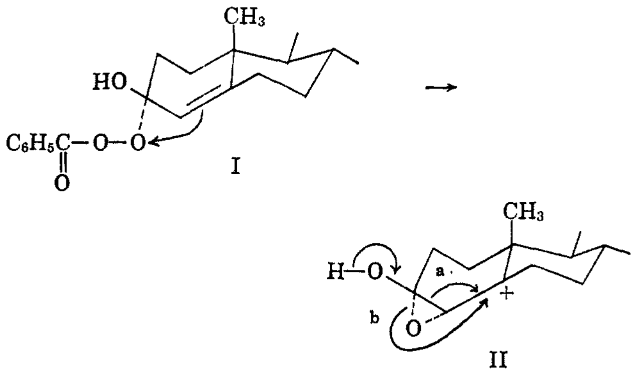
This might have arisen by oxidation of **15** formed by hydrolysis of formate **5** (Scheme IV). A similar oxidation of **15** to **14** has been described already in the literature.[21]

SCHEME IV



A reasonable reaction mechanism which would explain the formation of both enol lactone **2** and 4α,5α-epoxy ketone **6** from **1** involves axial α-side attack of the per acid on the protonated carbonyl function at C-3. The resulting intermediate (I) will be in a favorable conformation for the participation of the double-bond electrons, in the formation of a species (II, Scheme V).[22] The latter may for meither enol lactone **2** by the cleavage of C_3–C_4 bond (process a), or 4α,5α-epoxy ketone **6** by the cleavage of the C_3–O bond (process b). It may be stressed that peroxidation of testosterone in the presence of base leads to a mixture of both 4β,5β- and 4α,5α-epoxy ketones **12** and **6**, the former predominating.[8a]

SCHEME V



Experimental Section[14,16,17]

All melting points were taken in capillaries and were uncorrected, the infrared spectra were determined on a Perkin-Elmer Infracord, and the rotations were done in chloroform solution. Molecular weights were obtained from the mass spectral determinations.

Oxidation of Testosterone Acetate (1) with Perbenzoic Acid and Anhydrous Perchloric Acid. A.—Chloroform (95 cc) was shaken in a separatory funnel with perchloric acid (5 cc, 72%) for 2 min, after which the upper phase was separated and dried over sodium sulphate. Compound **1** (10 g) was dissolved in 55 cc of a solution containing 4.18 g of perbenzoic acid in chloroform (1 mole equiv of per acid), and treated with 45 cc of the previously prepared solution of chloroform and perchloric acid for 12 hr at room temperature. The material was isolated from ether, washed with sodium bicarbonate and sodium bisulfite solution, and evaporated to dryness under high vacuum to remove the methyl benzoate present in the reagent. The nmr spectrum of the product had signals assigned to the protons of **4a**, **2**, and **1** (Table I). This material was chromatographed on 300 g of silica. The first fraction eluted with pentane–ether (4:1) gave 0.3 g of **6**: mp 158–162° (after crystallization from ether), $[\alpha]_D$ −71° (lit.[8b] mp 164–165°, $[\alpha]_D$ −68°).

The second fraction, isolated from the same solvent mixture, was recrystallized from ether–pentane to give 1.38 g of **2**: mp 126–128°; λ_{max}^{KBr} 5.66, 5.77, and 6.08 μ; λ_{max}^{EtOH} 204 mμ (ε 10,000).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.71; H, 8.50.

B.—Compound **1** (5 g) was treated with 66 cc of chloroform containing 4.18 g of perbenzoic acid (2 mole equiv of per acid) and with 66 cc of chloroform containing dry perchloric acid (prepared as under A) for 12 hr at room temperature. The nmr spectrum of the isolated material had signals at 4.76, 3.03, and 10.2 assigned to protons of **3a**, **6**, and **7**, respectively; the area of these signals indicated that the amounts of the various products were 70, 10, and 11% of the total. The crude product was crystallized from ether–pentane to give 2.4 g of **3a** and **3b**, mp 114–120°. Three additional recrystallizations gave 0.3 g of the mixture: mp 133–134°, $[\alpha]_D$ +6°, mol wt 362, λ_{max}^{KBr} 5.66 and 5.75 μ.

Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.46; H, 8.36.

The mother liquor residue of the material (mp 114–120°) was recrystallized from the same solvent, to give **3a**: 0.5 g, mp 110–112°, mol wt 326, λ_{max}^{KBr} 5.64 and 5.75 μ.

The combined mother liquor residues were chromatographed on silica gel (100 g). Elution with pentane–ether (19:1) gave 0.31 g of **6**, mp 158–160°.

The second fraction eluted with pentane–ether (5:1) gave 1.22 g of **3a**, mp 108–112°, identical with the material obtained above.

The third fraction eluted with ether–pentane (5:1 and 4:1) gave 0.23 g of **7**: mp 93–94°, mol wt 394, λ_{max}^{KBr} 5.71 and 5.77 μ.

The fourth fraction eluted with ether gave 0.7 g of **4a**: mp 166–180°, $[\alpha]_D$ −4.5°, mol wt 362, λ_{max}^{KBr} 5.78 and 9.13 μ.

Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.05; H, 8.11.

C.—Compound **1** (1 g) was treated with a solution of perbenzoic acid (0.84 g, 2 mole equiv) and anhydrous perchloric acid in chloroform as under A for 84 hr. The nmr spectrum of the isolated material showed peaks assigned to **4a**, **4b**, **3a**, and **6**. Crystallization from ether–pentane gave 0.75 g of **3a** and **3b**, mp 116–118°. Fractional recrystallization from the same solvents yielded **3a**, mp 108–110°, and a 1:1 mixture of **3a** and **3b**, mp 133–134°.

D.—Compound **1** (5 g) was dissolved in 114 cc of chloroform containing 8.36 g of perbenzoic acid (4 mole equiv) and in 136 cc of chloroform containing dry perchloric acid. After 84 hr the isolated material was crystallized from ether–pentane to give 0.46 g of **4a**, mp 164–180°. The mother liquor residues were chromatographed on silica gel (150 g). The first fraction eluted with pentane–ether (6:1) gave 0.35 g of **6**, mp 158–162°.

The second fraction eluted with pentane–ether (4:1) gave 1.9 g of **3a**, mp 108–112°.

The third fraction eluted with pentane–ether (1:1) gave 0.45 g of **4b**: mp 156–162° (four recrystallizations from ether–pentane), $[\alpha]_D$ +89°, mol wt 362, λ_{max}^{KBr} 5.73 μ.

Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 7.34; H, 7.89.

The fourth fraction eluted with the same solvents gave 0.3 g of **5**: mp 174–178° (three recrystallizations from ether); $[\alpha]_D$ +26°; λ_{max}^{KBr} 5.75, 5.85, 8.06, and 8.75 μ.

Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.64; H, 7.99. Found: C, 66.27; H, 7.78.

17β-Acetoxymethyl Ester 10a. A.—A solution of 0.2 g of **4a** in 10 cc of acetone was oxidized with Jones reagent. Extraction with methylene chloride and with 10% sodium hydroxide solution yielded, beside recovered **4a** (0.14 g), 0.06 g of an acidic product. This was methylated with diazomethane, reacetylated with acetic anhydride and pyridine, and chromatographed on kieselgel (100 g). Elution with dioxane–hexane (5:1) gave 0.02 g of **10a**: mp 174–180° (crystallization from ether–methanol), $[\alpha]_D$ +37°, mol wt 392, λ_{max}^{KBr} 5.76 μ.

Anal. Calcd for $C_{22}H_{32}O_6$: C, 67.34; H, 8.22. Found: C, 67.45; H, 8.12.

B.—A solution of 2 g of **12** in 100 cc of isopropyl alcohol, 24.5 g of hydrazine hydrate (100%), and 1.1 cc of acetic acid was heated for 0.5 hr on a water bath, left at room temperature

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[22] A similar intermediate was postulated by E. Wenkert and M. Rubin [*Nature*, **170**, 708 (1952)] in the per acid oxidation of α-benzylidene ketones.

for 1 hr, poured into water, and extracted with methylene chloride. Chromatography on alumina (50 g) and elution with benzene gave 0.78 g of **11** (crystallized from ether): mp 118–119°, $[\alpha]_D$ +85°.

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 76.06; H, 9.57.

Compound **11** (0.35 g) was dissolved in 50 cc of chloroform, and a stream of ozone was passed through it at −15°. After 15 min, nitrogen was blown through the solution 5 cc of water being added to the heated solution. The solvent was evaporated, and the residue was dissolved in 5 cc of acetone and oxidized with Jones reagent. Extraction with ether and methylation with diazomethane gave a material which was chromatographed on kieselgel (100 g). Elution with hexane–ether (2:3) and crystallization from ether–pentane gave 0.035 g of **10a**, mp 176–180°, $[\alpha]_D$ +36°, identical with the material described under A.

17-Ketomethyl Ester 10b.—A solution of **4a** (0.2 g) in 10 cc of dioxane and 2 cc of sulfuric acid (20%) was treated under reflux for 3 hr. The isolated material was dissolved in 10 cc of acetone and oxidized with Jones reagent. Extraction with ether, methylation with diazomethane, and chromatography on kieselgel (50 g) using dioxane–hexane (5:1) as eluent gave 0.07 g of **10b**: mp 229–234° (crystallization from ether–pentane), $[\alpha]_D$ +90°, λ_{max}^{KBr} 5.79 μ.

Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.99; H, 7.99.

This compound was identical with a sample of **10b**:[12] mp 241–242°, $[\alpha]_D$ +95°.

Rearrangement of Epoxy Lactone 3a. A.—Compound **3a** (0.025 g) was heated at 160–180° for 15 min in an evacuated tube (20 mm). Three crystallizations from ether gave **4a**, mp 168–180°.

B.—A solution of **3a** (0.5 g) in 50 cc of benzene was treated with 2 cc of boron trifluoride etherate overnight at room temperature. The isolated material gave 0.21 g of **4a**, mp 168–180°.

C.—A solution of 0.2 g of **3a** in chloroform containing anhydrous perchloric acid was left for 48 hr at room temperature. The material isolated from ether was recrystallized from the same solvent to give 0.08 g of **4a**.

Rearrangement of the Mixture of Epoxy Ketones 3a and 3b. A.—Ketones **3a** and **3b** (mp 133–134°, 0.10 g) were heated in an evacuated tube (20 mm) for 15 min at 160–180°. Chromatography on alumina (30 g), and elution with pentane–ether (1:1) gave 0.015 g of **4a**, mp 168–180°. Elution with ether gave 0.02 g of **4b**, mp 158–162°.

B.—A solution of **3a** and **3b** (mp 133–134°, 0.02 g) in 5 cc of benzene was treated with 0.1 cc of boron trifluoride etherate overnight at room temperature. The isolated material showed nmr signals at 10.10 and 10.67 ppm (integration ratio 1:1) of **4a** and **4b**. The peaks at 4.76 and 4.66 ppm of **3a** and **3b** disappeared.

Conversion of 5α-Formate 5 to Enol Lactone 13.—Compound **5** (0.05 g) was heated for 25 min at 180° in an evacuated tube (25 mm) and chromatographed on 10 g of silica, and the fraction eluted with pentane–ether (9:1) gave 0.02 g of **13**: mp 128–129° (crystallization from pentane); λ_{max}^{KBr} 5.51, 5.72, and 5.85 μ (identical with an authentic sample) (lit.[17] mp 129–133°).

Oxidation of Enol Lactone 2 with Perbenzoic Acid and Anhydrous Perchloric Acid.—A solution of **2** (0.3 g) in 9 cc of chloroform containing anhydrous perchloric acid and in 6 cc of chloroform containing 0.26 g of perbenzoic acid (2.1 mole equiv) was left for 24 hr at room temperature. The nmr spectrum of the product had peaks at 4.76 and 10.10 ppm of **3a** and **4a**, respectively. The area of these signals indicated the respective amounts of **3a** and **4a** being 70 and 15% of the total.

Oxidation of Aldehydo Lactone 4a with Perbenzoic Acid and Anhydrous Perchloric Acid.—A solution of **4a** (0.2 g) in 10 cc of chloroform containing anhydrous perchloric acid and in 5 cc of chloroform containing 0.077 g of perbenzoic acid (1 mol equiv) was left for 48 hr. The isolated material showed nmr signals at 10.10 and 8.47 ppm of **4a** and **5**, respectively.

Oxidation of Testosterone Acetate with Perbenzoic Acid and Aqueous Perchloric Acid.—Chloroform (70 cc) was shaken in a separatory funnel with perchloric acid (5 cc, 72%) for 2 min after which the upper phase was immediately separated. Compound **1** (3 g) was dissolved in a solution of 33 cc of chloroform containing 2.5 g of perbenzoic acid (2 mole equiv), and treated with 67 cc of the previously prepared solution of chloroform and aqueous perchloric acid. After being left overnight, the material was isolated from ether and crystallized from ether–pentane to give 0.75 g of **8**: mp 176–178°, $[\alpha]_D$ +65°, λ_{max}^{KBr} 5.82 and 5.75 μ.

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.05. Found: C, 72.14; H, 8.96.

The mother liquor residues showed two spots on thin layer chromatography, comparable with those of **8** and **9**.

A solution of **8** (0.2 g) in 15 cc of dioxane, was treated with a solution of 2 g of potassium hydroxide in 15 cc of water, and heated under reflux for 4 hr. After acidification with hydrochloric acid (10%) and extraction with methylene chloride, the residue was crystallized from ether–methanol to give 0.15 g of **8** (17β-OH): mp 170–172°, $[\alpha]_D$ +85° (identical with an authentic specimen) (lit.[10] mp 178–179°, $[\alpha]_D$ +92°).

Conversion of Enol Lactone 2 to A-Nor Ketone 9.—A solution of **2** (0.1 g) in 10 cc of chloroform containing aqueous perchloric acid, was left at room temperature for 4 hr. The isolated material was chromatographed on silica gel (10 g). Elution with pentane–ether (9:1) gave 0.02 g of material, mp 121–140°, which after rechromatography on silica (5 g) gave 0.015 g of **9**, mp 138–140° (identical with an authentic sample) (lit.[9] mp 141–143°).

Oxidation of Testosterone Acetate (1) with *m*-Chloroperbenzoic Acid and Anhydrous Perchloric Acid. A.—A solution of **1** (2.5 g) and of *m*-chloroperbenzoic acid (6.14 g, 85%, 4 mole equiv) in 75 cc of chloroform was left for 12 hr. The isolated material showed in nmr spectrum signals at 4.76 and 10.10 ppm of **3a** and **4a** whose relative intensity corresponds to the former being 50% and the latter less than 10% of the total. Recrystallization from ether gave 0.62 g of **3a**, mp 108–112°.

B.—Compound **1** (2.5 g) was treated as before, but for 120 hr. The isolated material showed nmr peaks at 4.76 and 10.10 ppm of **3a** and **4a**, respectively, whose relative intensity corresponded to the former being 10 and the latter 30% of the total.

Oxidation of Testosterone Acetate with *m*-Chloroperbenzoic and Aqueous Perchloric Acid.—A solution of **1** (5 g) and 6.5 g of *m*-chloroperbenzoic acid (85%, 2.1 mole equiv) in 150 cc of chloroform containing aqueous perchloric acid, was left for 12 hr. The isolated material was chromatographed on silica (120 g). The first fraction eluted with pentane–ether (4:1) was recrystallized from pentane to give 0.2 g of **9**, mp 135–137°.

The second fraction eluted with pentane–ether (2:1) was dissolved in ether and extracted with sodium carbonate solution. The ether extract gave 0.1 g of **8**, mp 176–180°.

The third fraction isolated from pentane–ether (1:1) was recrystallized from ether and gave **4a**, mp 168–180°.

The fourth fraction, eluted with ether, was recrystallized from the same solvent, and yielded 0.3 g of **14**: mp 186–187°, $[\alpha]_D$ +1°, mol wt 366, λ_{max}^{KBr} 5.68 and 5.78 μ.

Anal. Calcd for $C_{20}H_{30}O_6$: C, 65.55; H, 8.25. Found: C, 65.24; H, 8.16.

Registry No.—I, 7484-17-5; **1**, 1045-69-8; **2**, 6218-22-0; **3a**, 7430-03-7; **6**, 5178-01-8; **3b**, 7430-05-9; **4a**, 7430-06-0; **7**, 7430-07-1; **4b**, 7430-08-2; **5**, 7430-09-3; **11**, 7430-10-6; **12a**, 5012-85-1; **12b**, 7430-11-7; **10a**, 7445-10-5; **10b**, 7445-11-6; **13**, 1458-92-0; **9**, 6181-55-1; **8**, 7484-24-4; **15**, 7430-16-3; **14**, 7445-07-0; perbenzoic acid, 93-59-4; acetone, 67-64-1; diazomethane, 463-60-5; acetic anhydride, 108-24-7; pyrimidine, 110-86-1; dioxane, 123-91-1; *m*-chloroperbenzoic acid, 937-14-4.