maxima at 432 mμ ($E^{1\%}_{1cm}$ 1490) and 457 mμ ($E^{1\%}_{1cm}$ 1213) (cyclohexane). *Anal.* Calcd for $C_{42}H_{58}O_4$: C, 79.45; H, 9.21; methoxyl, 9.77. Found: C, 79.46; H, 9.30; methoxyl, 9.81.

1,18-Bis(4-methoxy-2,6,6-trimethyl-1-cyclohexen-3-on-1-yl)-3,7,12,16-tetramethyl-1,3,5,7,11,13,15,17-octadecaoctaen-9-yne (XIV).—A solution of XIII (3.8 g) in toluene (200 ml) was added to a reaction flask containing cyclohexanone (100 ml) and aluminum isopropoxide (10 g), and the mixture was stirred at reflux under an atmosphere of nitrogen until tlc indicated that the oxidation was complete. The mixture was poured onto cold, dilute (5%) sulfuric acid and washed until neutral, and the solvent was distilled under vacuum. After recrystallization from benzene, XIV was obtained as a red, crystalline solid, 3.3 g (87%), mp 202°. *Anal.* Calcd for $C_{42}H_{54}O_4$: C, 80.97; H, 8.74. Found: C, 81.04; H, 9.01.

1,18-Bis(4-methoxy-2,6,6-trimethyl-1-cyclohexen-3-on-1-yl)-3,7,12,16-tetramethyl-1,3,5,7,9,11,13,15,17-octadecanonene (XV).—A suspension of XIV (2 g) in heptane (150 ml) was hydrogenated with Lindlar's catalyst by the procedure already described for the preparation of XIV. Recrystallization from methylene chloride–methyl alcohol afforded 1.5 g (75% of XV as red needles, mp 212°. The absorption spectrum had maxima at 467 (in cyclohexane) and 485 mμ (in pyridine). *Anal.* Calcd for $C_{42}H_{56}O_4$: C, 80.71; H, 9.04; methoxyl, 9.92. Found: C, 80.93; H, 9.21; methoxyl, 10.27.

Acknowledgment.—We wish to thank Dr. A. Steyermark and his staff for the microanalyses, Dr. F. Forrester and Mr. J. Volpe for the ultraviolet spectra, and Dr. F. Vane for the nmr spectrum.

Transformations of Fusidic Acid. III. 17-Oxa-4α,8,14-trimethyl-D-homo-18-norandrostanes[1,2]

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A new and unexpected series of compounds (**4**) containing a ring-D lactol acetate has been obtained from the ozonolysis of fusidic acid derivatives. Sodium borohydride reduction deacetoxylated these compounds and gave the ring D lactones (**8** and **9**). The epimerization of the 9β-11-keto lactones to the 9α derivatives has been carried out and the stereochemistry of the epimers demonstrated by molecular-rotation differences and ORD measurements. Differences of chemical reactivity in the 9α and 9β series have been observed. Nmr and infrared spectral data for these compounds have been presented.

The presence of a 17,20 double bond in fusidic acid[3] (**1a**) presents a convenient handle for the elimination of the side chain by ozonolytic techniques. This is the method which was used by Godtfredsen and co-workers[3a] in the course of the structure proof of fusidic acid and has been used in our laboratories as an entry to the novel 4,8,14-trimethyl-18-norandrostane series.[2b] At the outset of our work on the degradation of fusidic acid we found that in addition to the expected products (**3**), ozonolysis led to a new series of compounds whose structure and reactions are the basis of this paper. The starting materials used in this work consist of a variety of fusidic acid derivatives[1,2] which were prepared by standard procedures described in the Experimental Section.

When methyl 3α,16β-diacetoxy-11-keto-$\Delta^{17(20)}$-fusiden-21-oate (**2b**) was ozonized in glacial acetic acid at 10–15° rather than by the previously described[3a] conditions (at −70° in methylene chloride containing 1% pyridine), a crystalline product was isolated in 40% yield. The elemental analysis for this compound showed that it contained one more oxygen than expected product **3a**. On the basis of the analytical data and the spectral and chemical data to be described, this compound has been assigned structure **4a**. Its infrared spectrum showed the presence of four carbonyl functions at 5.62 (3-acetate), 5.67 (16-acetate), 5.78 (17a-carbonyl), and 5.88 μ (11-carbonyl). In addition, the nmr spectrum showed a single proton appearing as a triplet J = 6.5–7 cps centered at τ 3.54. This peak at low field indicates a proton attached to carbon bearing two oxygen functions and is reminiscent of that found by Lavie and co-workers[4] in the ring A lactol acetate **5** derived from euphol. In **5** the proton at C-1 resonates as a single peak at τ 3.58.

Subsequent to the isolation of the lactol acetate **4a** from the ozonolysis of **2b** in acetic acid, we found that it was also formed during ozonolysis using Godtfredsen's conditions. Although expected diacetoxy diketone **3a** could not itself be isolated from the ozonolysis reaction, its presence in at least 30% yield was shown by its reductive deacetoxylation with zinc in refluxing acetic acid to the known[2a] acetoxy diketone **6a**. In addition to **6a**, lactol acetate **4a** (unaffected by the zinc–acetic acid treatment) was isolated from this reaction in 5% yield.

Similar results to those described above were obtained from ozonolysis of 3-keto compounds. Thus, when 3,11-diketone **1b** derived from fusidic acid, or its methyl ester (**1c**), was ozonized in acetic acid, a 30–35% yield of the lactol acetate **4b** was obtained. This compound had a peak at τ 7.84 in the nmr spectrum (16β-acetate protons) and the 16α proton appeared as a multiplet centered at τ 3.54. When the ozonolysis was carried out in methylene chloride, known acetoxy triketone **3b** was obtained in 46% yield. Godtfredsen reports[3a] that this compound has a melting point of 211.5–212.5°. We have found that the melting range of acetoxy triketone, isolated in different runs and having identical infrared spectra, varied from 184–186° to 224–226°. It is our belief that small amounts of lactol acetate **4b**, mp 255–257°, in these samples are responsible for the variable melting point behavior,

(1) A preliminary report on this work was presented at the 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, Abstracts, p 20P.

(2) (a) Paper I: P. A. Diassi, G. W. Krakower, I. Bacso, and H. A. Van Dine, *Tetrahedron*, **22**, 3443 (1966). (b) Paper II: P. A. Diassi, I. Bacso, G. W. Krakower, and H. A. Van Dine, *ibid.*, **22**, 3459 (1966).

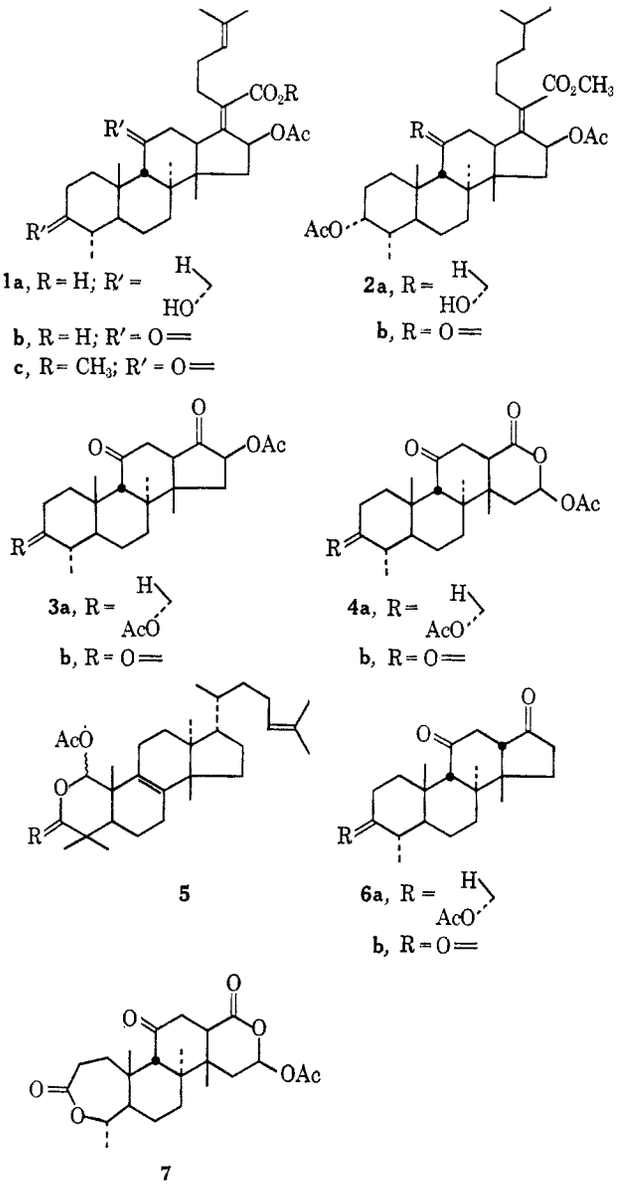
(3) (a) W. O. Godtfredsen and S. Vangedal, *ibid.*, **18**, 1029 (1962); (b) W. O. Godtfredsen, W. von Daehne, S. Vangedal, A. Marquet, D. Arigoni, and A. Melera, *ibid.*, **21**, 3505 (1965).

(4) D. Lavie, E. Glotter, and Y. Shvo, *ibid.*, **19**, 1377 (1963).

and, indeed, when a sample of acetoxy triketone, mp 189–191°, was deacetoxylated with zinc in refluxing acetic acid, beside expected triketone **6b**, a 2.5% yield of **4b** was obtained.

In order to determine if the "normal" ozonolysis products (**3**) are precursors of the lactol acetates (**4**), acetoxy triketone **3b** was subjected to ozonation in glacial acetic acid. Since only unchanged starting material was recovered from this experiment, it is evident that the lactol acetate is not formed by further attack of ozone on the ring D ketol acetate moiety of **3**. The mechanism for the formation of the lactol acetates probably involves the fragment obtained from the side chain during ozonolysis. The intermediate ozonide b formed by addition of ozone to the double bond of a breaks down to form the ketol acetate c and the dipolar dioxide d. These types of intermediates have been proposed by Criegee[5] in his studies of the mechanism of ozonolysis. The negatively charged oxygen of d (or its protonated counterpart) could attack the carbonyl to give the intermediate e which would then collapse to give the protonated lactol acetate f and then the lactol acetate g. The steps from c to g are analogous to those in the Baeyer–Villiger reaction[6,7] (Scheme I, p 186). An intermediate similar to e has been proposed by Bailey[8] to explain products obtained from the low-temperature ozonolysis of naphthalene. It is assumed of course that the migration of C-16 to oxygen proceeds with retention of configuration as in the Baeyer–Villiger reaction.[6]

In an attempt to prepare **4b** directly by the Baeyer–Villiger reaction, acetoxy triketone **3b** was treated with *m*-chloroperbenzoic acid. However, tlc showed that after 3 hr a more polar product than lactol acetate **4b** was forming. Not unexpectedly, it was found that attack on ring A occurred before insertion of oxygen into ring D was completed. After overnight reaction, therefore, the product isolated was the ring A lactone, ring D lactol acetate **7**. Reaction of the crude ozonolysis product containing a mixture of ketol acetate **3b** and lactol acetate **4b** with *m*-chloroperbenzoic acid also gave **7** in 41% yield. The assignment of structure **7** to this product is supported by its nmr spectrum. Thus, the 16α proton is found at low field (τ 3.53) showing the insertion of oxygen between C-16 and C-17 rather than between C-13 and C-17.[9] The presence of oxygen between C-3 and C-4 is shown by the downfield shift of the 4α-methyl doublet to τ 8.66 from 8.93 in **4b**. The presence of only a single proton at τ 5.55, rather than the two protons that would be present if migration of the C-2–C-3 bond had taken place, also supports this assignment. This is entirely consistent with the findings of Rosenthal, *et al.*,[10] that, in the Baeyer–Villiger oxidation of 4-methyl-3-keto steroids, the more substituted C-4 rearranges almost exclusively.

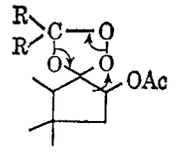


Additional evidence for the structures of lactol acetates **4a** and **4b** was obtained from the course of their reaction with sodium borohydride in ethanol. This reduction led to 3α-acetoxy-11α-hydroxy lactone (**8b**) and 3β,11α-dihydroxy lactone **9a**, respectively. In contrast to Lavie and co-workers,[4] we found no trace of reduction of the lactone group to hemiacetal. The nmr spectra of **8b** and **9a** show the disappearance of the acetate protons in the τ 7.85 region, and of the triplet at 3.54. The C-16 protons now appear as a multiplet at τ 5.64. Acetylation of **9a** gave 3β-acetate **9b** and oxidation of **8b** and **9a** gave 3α-acetoxy-11-keto lactone **10** and 3,11-diketo lactone **11**, respectively.

(5) R. Criegee, A. Kerakow, and H. Zinke, *Chem. Ber.*, **88**, 1878 (1955), and previous papers; R. Criegee, *Rec. Chem. Progr.*, **18**, 111 (1957).

(6) For a recent discussion of the mechanism of the Baeyer–Villiger reaction, see P. A. S. Smith in "Molecular Rearrangements," Part I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter 8.

(7) It has recently been suggested [H. Kwart and D. M. Hoffman, *J. Org. Chem.*, **31**, 419 (1966)] that per acid epoxidations of olefins may involve a 1,3-dipolar addition step. If these authors' conclusions are relevant to the present case, the intermediate formed by c and d may be the dipolar addition product i which would rearrange as shown to give the final product g.



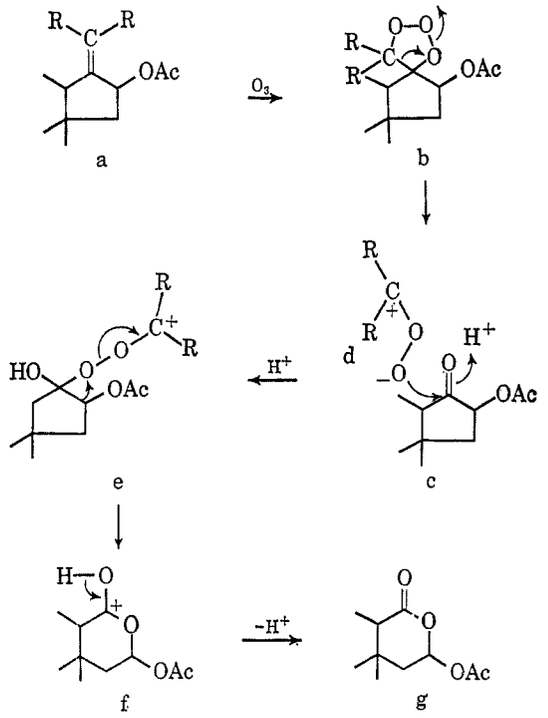
i

(8) P. S. Bailey and F. J. Garcia-Sharp, *ibid.*, **22**, 1008 (1957).

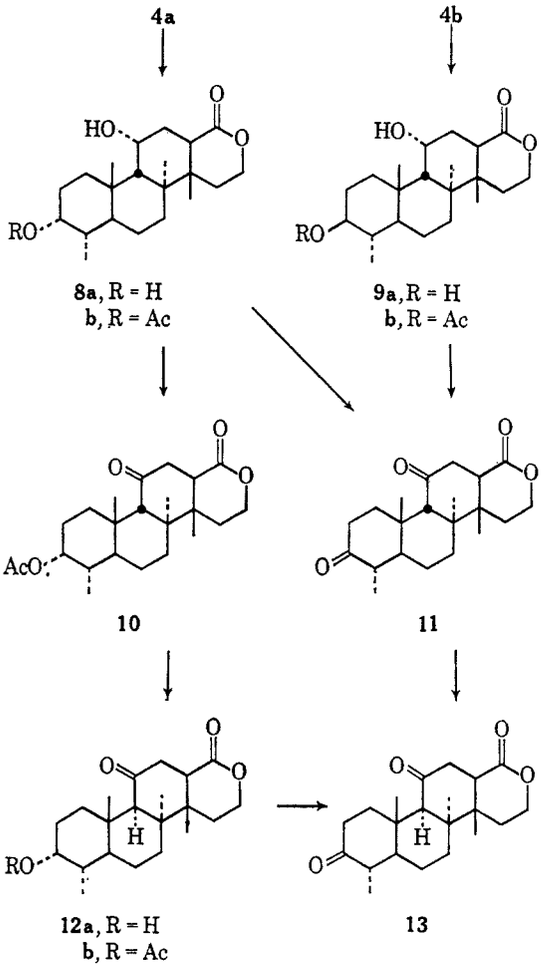
(9) The migration of a methine carbon in which one of the substituents is an acetoxyl group in preference to an ordinary methine group would be expected if migratory aptitude is based on the ability of the migrating group "to sustain a positive charge:" ref 6, p 585.

(10) D. Rosenthal, A. O. Niedermayer, and J. Fried, *J. Org. Chem.*, **30**, 510 (1965).

SCHEME I



SCHEME II



The 3α-acetoxy and 3-keto series were interrelated by saponification of **8b** to give 3α,11α-dihydroxy lactone **8a**, which was oxidized to 3,11-diketo lactone **11** (see Scheme II).

When diketo lactone **11** was refluxed in ethanolic potassium hydroxide a new diketo lactone (**13**) was isolated after reacidification. Similarly, acetoxyketo lactone **10** was converted to deacetylated epimeric 3α-hydroxy-11-keto lactone **12a** by refluxing ethanolic potassium hydroxide and reacidification. Acetylation of **12a** gave epimeric acetoxyketo lactone **12b** and oxidation gave epimeric diketo lactone **13** described above. Godtfredsen and co-workers have reported[3] the epimerization of 11-ketofusidic acid derivatives bearing a fully saturated side chain. The molecular rotation differences of these epimeric 9α-11-ketofusidic acid derivatives are shown in Table I. A previous paper from these laboratories[2a] describes the preparation of the four 9,13-epimers of 4α,8,14-trimethyl-18-norandrostane-11,17-diones derived from fusidic acid

TABLE I

MOLECULAR ROTATION DIFFERENCES OF 9,13-EPIMERIC FUSIDIC ACID DERIVATIVES[a]

Compd	ΔM_D, deg: 9α,13α–9β,13α	9β,13β–9β,13α	9α,13β–9β,13α
3α-Acetoxy-4α,8,14-trimethyl-18-norandrostane-11,17-dione[b]	−765	+289	−311
4α,8,14-Trimethyl-18-norandrostane-3,11,17-trione[b]	−1010	+309	−610
Methyl 16β-hydroxy-3,11-diketofusidan-21-oate[c]	−971		
16β-Acetoxy-3,11-diketofusidan-21-oic acid[d]	−955		
3,11,16-Triketo-fusidan-21-oic acid[d]	−962		
Methyl 3α,16β-dihydroxy-11-ketofusidan-21-oate[e]	−720		

[a] All rotations are reported in chloroform. [b] Reference 2a. [c] Dr. W. O. Godtfredsen, private communication. [d] Reference 3a. [e] Reference 3b.

in both the 3-acetoxy and 3-keto series. The molecular rotation differences of these epimers compared with those of the 9β,13α compounds also appear in Table I. In the present case, the molecular rotation differences of the pairs **10**–**12b** and **11**–**13** are −665° and −885°, respectively.[11]

Since, as can be seen from Table I, epimerization of the 9β proton to 9α involves a strong levorotatory shift, and since in all previous cases studied the 9α epimer is by far the more stable,[2a,3b] it can be stated without hesitation that the present case involves epimerization at C-9. From the molecular rotation data alone, though, we cannot specifically say that the epimers still retain the trans CD ring juncture. Although, the molecular rotation differences seen in this case are consistent with those observed for 9β,13α to 9α,13α epimerization, the effect of the six-membered ring D compared with that of the normal five-membered ring D on the magnitudes of this levorotatory shift cannot be assessed.

An examination of the conformational factors operating in this epimerization does not permit the conclusive assignment of the C-13 stereochemistry, either. Since the epimeric lactones are hydrolyzed readily in

(11) (a) It is interesting to note that, in this case and in the examples shown in Table I, the magnitude of the differences in the 3-keto compounds is greater by 200–250° than for the corresponding 3α-hydroxy or acetoxy compounds. (b) It might also be argued that, if the rate of equilibration of the open form was rapid compared with lactonization and the rates of lactonization of the two epimers differed greatly, the product would be determined kinetically rather than thermodynamically. In any case, an *a priori* prediction of the stereochemistry at C-13 cannot be made.

dilute base at room temperature, there is no question that under epimerizing conditions they exist as the open δ-hydroxycarboxylic acid anions. Therefore, the equilibration at C-13 under consideration does not involve a *cis vs. trans* decalin system but rather the preferred orientation of a cyclohexane carboxylate anion.[11b] Since ring C is now flexible, it is difficult to assign a specific configuration (axial or equatorial) to the carboxylate group. About all that can be said with certainty is that the carboxylate must be in a position in which it is readily lactonized, since we have not been able to isolate free hydroxy acid from the reaction mixture even on careful neutralization of the reaction.

In the absence of a clear-cut indication of the stereochemistry at C-13 of the epimeric lactones, a chemical solution for this problem was sought. We had previously[2a] had success in a similar situation by eliminating the asymmetric center at C-9, through introduction of a 9(11) double bond. The stereochemistry at C-13 could be then established by the identity or nonidentity of the $\Delta^{9(11)}$ compound derived from the epimer. The same approach was used in the present case. Thionyl chloride–pyridine treatment of 3β-acetoxy-11α-hydroxy 9β-lactone **9b** gave 3β-acetoxy $\Delta^{9(11)}$-lactone **14b** (Scheme III).

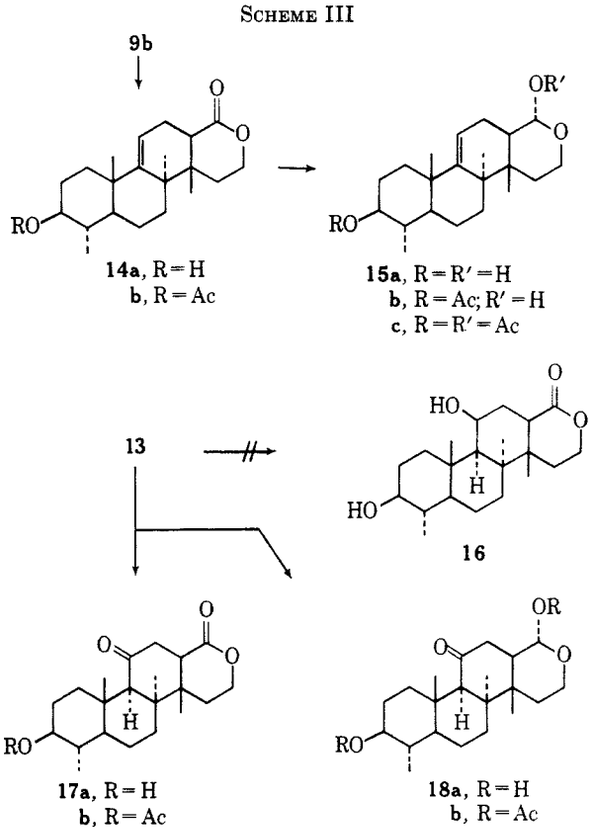
In order to prepare a $\Delta^{9(11)}$ derivative from the 9α series, 3,11-diketo 9α-lactone **13** had to be reduced. This reduction led to some unexpected and interesting results. When **13** was treated with sodium borohydride in ethanol, a product was obtained which was thought at first, although with some reservations, to be desired 3β,11β-dihydroxy 9α-lactone **16**. Its infrared spectrum showed the presence of two hydroxyl groups at 2.8 and 3.0 and a carbonyl function at 5.90 μ. The wavelength of the latter function is somewhat unusual for a six-membered lactone since we have consistently seen this grouping at 5.80–5.85 μ in the present study. Acetylation of this compound showed that our reservations were justified. The isolated product had an infrared spectrum which did not exhibit any hydroxyl peaks and had three carbonyl peaks. This, of course, ruled out the presence of an 11β-hydroxyl group in the reduction product, since this group is hindered and not acetylable under the usual conditions.[2a] The nmr spectrum showed the presence of two acetate methyls at τ 7.91 and 7.94, and significantly a single proton appeared as a doublet (J = 7.5 cps) at τ 4.14. The structure that has been assigned to this compound is **18b**, a 3β-acetoxy-11-keto-9α-hemiacetal acetate, and the peak at τ 4.14 is assigned to the C-17a-hemiacetal proton, coupled to the C-13 proton. The reduction product is, therefore, 3β-hydroxy-11-keto-9α-hemiacetal **18a**.

Acetylation of the mother liquors of the reduction product gave a new compound which had only one acetate methyl group at τ 7.94 in the nmr spectrum and no protons below 5.0. We have characterized this as 3β-acetoxy-11-keto 9α-lactone **17b**, arising from the reduction of the 3-ketone only. An identical product was obtained by reducing **13** with sodium borohydride in ethanolic potassium hydroxide. The isolated product was 3β-hydroxy-11-keto 9α-lactone **17a**, which gave **17b** on acetylation. This reduction took a different course since the lactone was opened to the hydroxy acid in the strongly basic reaction mixture, and was, therefore, not reduced by the borohydride. The lactone then re-formed on acidification during the work-up of the reaction.

The reduction of a six-membered steroidal lactone to the hemiacetal has been observed in a number of cases using a variety of reducing agents.[4,12–15] In some instances the reduction leads to both isomers,[12,14] whereas, in other cases only a single epimer has been observed.[4,13,15] The isolation of a single epimer in our case, coupled with the fact that it has not been observed to mutarotate in methanolic solution, would suggest that the more stable epimer is isolated in this case. Regardless, of the stereochemistry at C-13, this epimer can be assigned the 17aα-hydroxyl configuration. Models show that when the angular methyl group at C-14 is placed in an equatorial configuration on ring D severe steric interactions are introduced into the molecule. Therefore, a β-hydroxyl at C-17a will be 1,3-diaxially opposed to the preferred axial 14β-methyl group.

As was seen from the borohydride reductions of the lactol acetates **4**, the lactone group in the 9β series is uneffected by ethanolic sodium borohydride treatment. Similarly, $\Delta^{9(11)}$-lactone **14b** was recovered unchanged from overnight treatment with ethanolic sodium borohydride. However, when **14b** was treated with sodium borohydride in aqueous dioxane, the lactone was reduced and the 3-acetate was partially hydrolyzed to give a mixture of **15a** and **15b**. Acetylation of the total reduction mixture gave 3β-acetoxy-

SCHEME III



(12) G. R. Pettit, J. C. Knight, and W. J. Evers, *Can. J. Chem.*, **44**, 807 (1966), and previous paper.
(13) J. S. Baran, *J. Org. Chem.*, **30**, 3564 (1965).
(14) J. T. Edward, P. F. Morand, and I. Puskas, *Can. J. Chem.*, **39**, 2069 (1961).
(15) N. W. Atwater, *J. Am. Chem. Soc.*, **83**, 3071 (1961).

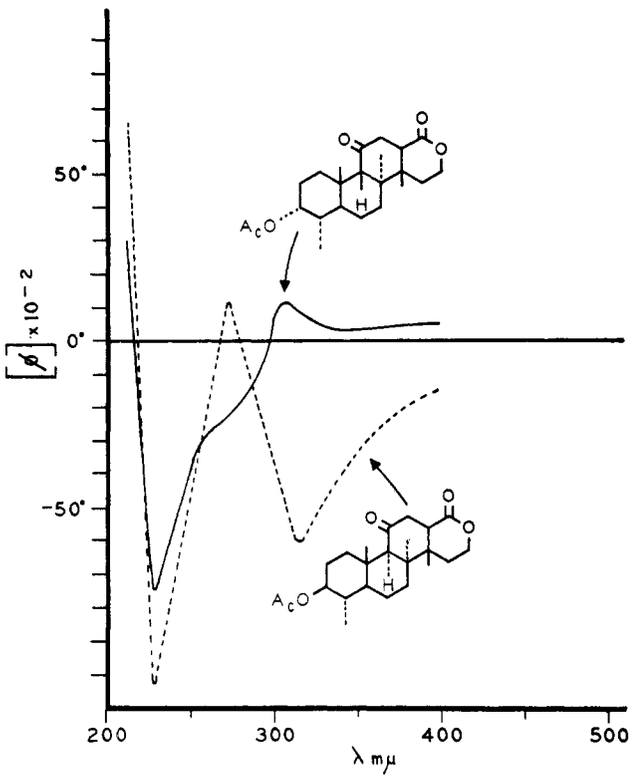


Figure 1.—Optical rotatory dispersion curves of 3α-acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,14β-androstane-11,17a-dione (**10**) (———) and 3β-acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androstane-11,17a-dione (**17b**) (- - - -).

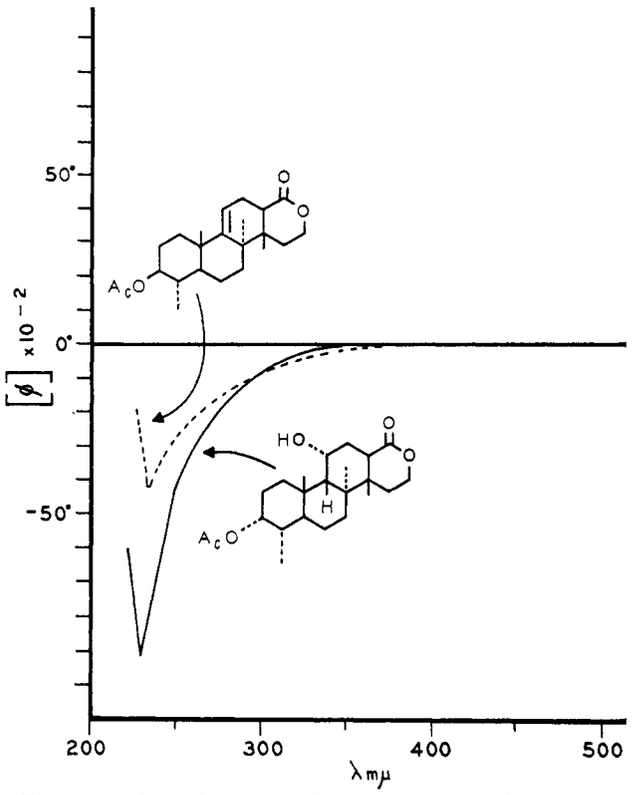


Figure 2.—Optical rotatory dispersion curves of 3α-acetoxy-11α-hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,-13α,14β-androstan-17a-one (**8b**) (———) and 3β-acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androst-9(11)-en-17a-one (**14b**) (- - - -).

$\Delta^{9(11)}$-hemiacetal acetate **15c**. The C-17a proton appeared as a doublet (J = 7.5 cps) at τ 6.27 and at 5.82 in the nmr spectra of **15a** and **15c**, respectively. The recovery of only one C-17a epimer from this reduction again indicates that the isolated product is the α-ol, the more stable of the two possible epimers (see Scheme III).

In addition to seeking a chemical solution to the stereochemistry of the C-13 position in the epimeric lactones, we also felt that Klyne's recently proposed "lactone sector rule"[16] might provide the answer to the stereochemical problem we faced. This rule which complements the "octant rule"[17] can be used to determine the stereochemical environment of a six-membered lactone from the sign of the ORD curve. Accordingly, the optical rotary dispersion curves of the lactones **10** and **17b** were determined and are shown in Figure 1.[18] In addition the ORD curves of the lactones **8b** and **14b** are shown in Figure 2.[18] From the latter figure it can be seen that both **8b** and **14b** have curves with a single extremum at 230 and 234 mμ, respectively. The lactone sector rule does predict a negative curve for these compounds, based on their known stereochemistry and shows the correctness of this rule in a novel stereochemical situation. The curves of **10** and **17b** (Figure 1) show two extrema, since they have an 11-ketone in addition to the lactone chromophore. Thus, 9β,11-keto derivative **10** has a peak at 315 and 9α-11-ketone **17b** has a trough at 316 mμ in addition to the lower wavelength troughs associated with the lactone grouping. This is entirely consistent with the previously reported dispersion curves of 9α- and 9β-11-keto derivatives of fusidic acid.[2a,3b] The lower wavelength trough in both **10** and **17b** indicates that the stereochemical environment of these two compounds is similar. Thus, the ORD determinations strongly support the presence of an unepimerized C-13α proton in **17b** and the other 9α derivatives described in this paper.[19]

(16) J. P. Jennings, W. Klyne, and P. M. Scopes, *Proc. Chem. Soc.*, 412 (1964); *J. Chem. Soc.*, 7211, 7229 (1959); W. Klyne, P. M. Scopes, and A. Williams, *ibid.*, 7237 (1965).

(17) W. Moffitt, A. Moscowitz, R. B. Woodsard, W. Klyne, and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 4013 (1961).

(18) We are grateful to Professor W. Klyne, Westfield College, London, for his kindness in determining these ORD curves.

Experimental Section

Melting points are uncorrected. The infrared spectra were taken on pressed potassium bromide pellets with a Perkin-Elmer Model 21 spectrophotometer. Optical rotations were taken in chloroform solution unless otherwise noted at room temperature on a Perkin-Elmer Model 141 polarimeter. Nmr spectra were measured in deuteriochloroform solution using tetramethylsilane as an internal standard on a Varian Associates A-60. As usual, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad.[20] Solutions were dried over magnesium sulfate prior to evaporation.

(19) We are grateful to a referee for bringing to our attention a recent paper (H. Wolf, Abstracts of the Proceedings of the 2nd International Congress on Hormonal Steroids, Milan, Italy, May 1966, paper 159, p 111) in which the statement is made that "the sign of the n–π* Cotton effect curves in the ORD spectra of some lactones (with strong background rotation) only can be determined by comparison with the CD spectra." A similar conclusion was reached by this author in a previous note: H. Wolf, *Tetrahedron Letters*, 1075 (1965).

(20) We have designated triplet and quartet to coupled protons whose apparent patterns fit these designations. It should therefore be understood that these coupling patterns have not been completely analyzed and the constants presented are done to permit the reader to reconstruct the general pattern of the curve.

16β-Acetoxy-3,11-diketo-$\Delta^{17(20),24}$-fusidadien-21-oic Acid (1b).—A solution of 10.00 g of fusidic acid (**1a**) in 250 ml of acetone was oxidized with 10 ml of chromic acid–sulfuric acid reagent.[21] After 30 min at room temperature the excess oxidizing agent was reduced with methanol. Some insoluble material was filtered, and water was added to the filtrate until crystallization started. Two crops of acid **1b**, 6.72 g, mp 207–210°, were collected and combined. Recrystallization from acetone–hexane gave analytically pure material: mp 211–212°; $[\alpha]_{589}$ +120°, $[\alpha]_{578}$ +124°, $[\alpha]_{546}$ +143°, $[\alpha]_{436}$ +272°, $[\alpha]_{365}$ +531°; λ_{max} 5.85–5.90, 8.0 (br) μ.

Anal. Calcd for $C_{31}H_{44}O_6$: C, 72.62; H, 8.65. Found: C, 72.71; H, 8.62.

Methyl 16β-Acetoxy-3,11-diketo-$\Delta^{17(20),24}$-fusidadien-21-oate (1c). A.—A suspension of 423 mg of **1b** in 50 ml of ether was treated with an excess of ethereal diazomethane. After reaction was complete, helium was bubbled through the solution to remove excess diazomethane, and evaporation of the solvent gave 439 mg of the methyl ester **1c**. The analytical sample was recrystallized from methanol–water and had mp 127–129°; $[\alpha]_{589}$ +118°, $[\alpha]_{578}$ +119°, $[\alpha]_{446}$ +137°, $[\alpha]_{436}$ +258°, $[\alpha]_{365}$ +504°; λ_{max} 5.74, 5.81, 5.88, 8.06 μ.

Anal. Calcd for $C_{32}H_{46}O_6$: C, 72.97; H, 8.80. Found: C, 72.94; H, 8.76.

B.—A solution of 10.00 g of fusidic acid, sodium salt, in 20 ml of methyl iodide and 100 ml of methanol was refluxed for 21 hr. The solvent was evaporated and the residue was taken up in methylene chloride and washed with 5% sodium bicarbonate and water and dried. Evaporation of the solvent gave 10.30 g of highly colored material which was dissolved in chloroform and passed through a column of 40 g of neutral alumina (activity I). The column was eluted with benzene which when evaporated gave 9.20 g of material. On recrystallization from acetone–hexane, 6.39 g of methyl fusidate was obtained.

A solution of the 6.39 g of methyl fusidate in 100 ml of acetone was oxidized at room temperature with an excess of chromic acid–sulfuric acid reagent.[21] The excess reagent was decomposed with methanol and the solution was diluted with water. After evaporation of the acetone, the organic material precipitated as a gum. This gum was separated and dissolved in ethyl acetate, and the solution was washed with saturated sodium chloride solution, dried, and evaporated to give 5.60 g of partially crystalline material. Recrystallization of this material from methanol–water gave **1c**, mp 127–129°, identical in all respects with the material prepared above.

Methyl 3α,16β-Diacetoxy-11α-hydroxy-$\Delta^{17(20)}$-fusiden-21-oate (2a).—A solution of 2.50 g of methyl 3-acetyl fusidate[3a] in 35 ml of 95% ethanol containing 500 mg of 5% palladium on calcium carbonate was hydrogenated at room temperature. After 1 mole of hydrogen was taken up (2 hr) the mixture was filtered and the solvent was evaporated. Recrystallization of the residue from acetone–hexane gave 1.86 g of **2a**, mp 142–145°. The sample prepared for analysis had mp 142–144°; $[\alpha]_{589}$ −17°, $[\alpha]_{578}$ −18°, $[\alpha]_{546}$ −20°, $[\alpha]_{436}$ −31°, $[\alpha]_{365}$ −36°; λ_{max} 2.80, 5.80, 8.05 μ.

Anal. Calcd for $C_{34}H_{54}O_7$: C, 71.04; H, 9.47. Found: C, 70.94; H, 9.30.

Methyl 3α,16β-Diacetoxy-11-keto-$\Delta^{17(20)}$-fusiden-21-oate (2b).—A slight excess of chromic acid–sulfuric acid reagent[21] was added to a solution of 1.722 g of **2a** in 25 ml of acetone kept below 20° and under an atmosphere of helium. After 15 min the excess chromic acid was decomposed by the addition of methanol. Water was then added and the acetone was evaporated. The aqueous residue was extracted with chloroform and the chloroform was washed with water, dried, and evaporated to give 1.734 g of material. Recrystallization from acetone–hexane gave 1.211 g of **2c**, mp 122–126°. The analytical sample had mp 123–124°; $[\alpha]_{589}$ +38°, $[\alpha]_{578}$ +40°, $[\alpha]_{546}$ +47°, $[\alpha]_{436}$ +94°, $[\alpha]_{365}$ +196°; λ_{max} 5.80, 5.90 (sh), 8.0–8.2 μ.

Anal. Calcd for $C_{34}H_{52}O_7$: C, 71.29; H, 9.15. Found: C, 71.28; H, 9.11.

3α,16β-Diacetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,14β-androstane-11,17a-dione (4a). A. Ozonolysis of 2b in Acetic Acid.—A solution of 5.72 g of **2b** in 125 ml of acetic acid was cooled to 10° and 110 mmoles of ozone was passed through in 75 min. The solution was kept at room temperature for 1 hr with helium bubbling through and the acetic acid was then evaporated.

Trituration of the resulting yellow oil with hexane–ether gave 2.35 g of white, crystalline material, mp 207–213°. The analytical sample of **4a** recrystallized from methanol had mp 218–219°; $[\alpha]_{589}$ −31°, $[\alpha]_{589}$ −33°, $[\alpha]_{578}$ −38°, $[\alpha]_{436}$ −65°, $[\alpha]_{365}$ −86°; λ_{max} 5.62, 5.67, 5.78, 5.88, 7.99 μ; nmr τ 3.54 (t, J = 6.5 and 6.5 cps, 16α-H), 5.05 (3β-H), 7.86 (16β-OAc), 7.93 (3α-OAc).

Anal. Calcd for $C_{25}H_{36}O_7$: C, 66.94; H, 8.09; acetyl, 19.19. Found: C, 67.09, 66.85; H, 8.26, 7.90; acetyl, 19.78.

B. Ozonlysis of 2b in Methylene Chloride.—A solution of 5.92 g of **2b** in 250 ml of methylene chloride containing 2.5 ml of pyridine was cooled to −70°. A stream of oxygen–ozone containing 50 mmoles of ozone was passed through the solution and it was then stirred for 90 min with 7.5 g of zinc dust and 12.5 ml of glacial acetic acid. The solution was filtered, washed with water, 5% sodium bicarbonate, and water, dried, and evaporated to give 6.05 g of a viscous, brown oil. Since no crystalline material could be obtained from this oil it was refluxed with zinc dust (12.0 g) in acetic acid (100 ml) for 4 hr. The zinc was filtered and washed with methylene chloride, the combined filtrate and washings were evaporated, and the residue was dissolved in methylene chloride. After washing successively with water and 5% sodium bicarbonate solution, the solvent was dried and evaporated to give 5.55 g of material. Recrystallization from ether gave a first crop of 1.074 g of 3α-acetoxy-11,17-dione **6a**, mp 185–186°, corresponding to a yield of at least 29% of **3a** in the ozonolysis reaction. The second crop consisted of 261 mg of **4a**, mp 209–211° (5% yield). The infrared spectrum of this material was identical with that obtained in the previous experiment.

16β-Acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,-9β,13α,14β-androstane-3,11,17a-trione (4b). A. Ozonolysis of 1c in Acetic Acid.—In a typical experiment, 200 l. of oxygen containing 200 mmoles of ozone was passed through a solution of 10.10 g of **1c** in 200 ml of acetic acid cooled to 5–10°. The reaction mixture was brought to room temperature with helium bubbling through the solution to remove excess ozone. After 1 hr the solvent was evaporated and the residue was taken up in ethyl acetate and washed with water and bicarbonate solution. The solution was dried and evaporated to give 7.20 g of residue which on recrystallization from methanol gave **4b** (3.09 g) in two crops, mp 247–251°. The analytical sample had mp 255–257°; $[\alpha]_{589}$ +54°, $[\alpha]_{578}$ +62°, $[\alpha]_{546}$ +66°, $[\alpha]_{426}$ +125°, $[\alpha]_{365}$ +244°; λ_{max} 5.70, 5.87, 8.26 μ; nmr τ 3.54 (m, 16α-H), 7.84 (16β-OAc).

Anal. Calcd for $C_{28}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 68.26; H, 7.95.

The first time this compound was prepared it was obtained in a different crystalline modification: mp 246–249°; λ_{max} 5.67, 5.75, 5.89, 8.23 μ. The infrared spectrum of a chloroform solution, as well as the nmr spectra of this and the previously described preparation, was identical.

B. Ozonolysis of 1b in Acetic Acid.—Following the procedure described above, 10.86 g of **1b** in 250 ml of acetic acid cooled to 10° was treated with 260 mmoles of ozone to give 6.40 g of residue. Recrystallization from methanol gave a first crop consisting of 2.64 g of lactol acetate **4b**, mp 252–255°, whose infrared and nmr spectra were identical with those of the previously obtained **4b**, and a second crop of 947 mg of material, mp 195–200°, whose infrared spectrum showed it to be impure ketol acetate **3b**.

Ozonolysis of 3b.—Six mmoles of ozone was passed through a solution of 100 mg of **3b** in 10 ml of glacial acetic acid at 15°, during 30 min. The solvent was evaporated, the residue was taken up in methylene chloride, washed with water, and dried, and the methylene chloride was evaporated. The residue of 101 mg was crystallized from methanol and then 95% ethanol to give 58 mg of material, mp 184–186°, whose infrared spectrum was identical with that of starting material. Thin layer chromatography of the crystalline material and the mother liquors confirmed that there was no conversion of starting material into lactol acetate **4b**.

16β-Acetoxy-4aα,8,14-trimethyl-4,17-dioxa-A,D-bishomo-18-nor-5α,8α,9β,13α,14β-androstane-3,17a-dione (7). A.—A solution of 194 mg of **3b**, mp 212–214°, and 345 mg of *m*-chloroperbenzoic acid in 10 ml of methylene chloride was kept in the dark at room temperature for 65 hr. The crystalline material which settled out of the solution (107 mg of *m*-chlorobenzoic acid, mp

(21) A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 2548 (1953).

151–152°) was filtered and washed with benzene. The filtrate and washings were diluted with benzene and washed successively with 5% potassium iodide, 5% sodium sulfite, saturated sodium chloride, 5% potassium bicarbonate, and saturated sodium chloride solutions. After drying, the solvent was evaporated to give 200 mg of residue, which on recrystallization from methanol gave 122 mg of **7**, mp 222–224°. The analytical sample had mp 229–231°; $[\alpha]_{589}$ +21°, $[\alpha]_{578}$ +22°; $[\alpha]_{546}$ +25°, $[\alpha]_{436}$ +26°, $[\alpha]_{365}$ +50°; λ_{max} 5.60, 5.80 μ; nmr τ 3.53 (q, J = 5.0 and 8.0 cps; 16α-H), 5.55 (m, 4aβ-H), 7.85 (16β-OAc), 8.66 (d, J = 7 cps, 4a-Me).

Anal. Calcd for $C_{23}H_{32}O_7$: C, 65.69; H, 7.67. Found: C, 65.70; H, 7.73.

B.—Impure **3b** (1.5 g of material, obtained from the ozonolysis of **1b** and contaminated with lactol acetate **4b** as shown by nmr spectrum) was treated with *m*-chloroperbenzoic acid (2.67 g in 37 ml of methylene chloride) and worked up as described above. From this reaction was obtained 842 mg of **7**, mp 229–232° (infrared spectrum identical with that of the previously obtained material).

3α-Acetoxy-11α-hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,14β-androstan-17a-one (8b).—A suspension of 250 mg of **4a** in 25 ml of absolute ethanol was treated with 125 mg of sodium borohydride and stirred at room temperature. After 10 min the substrate dissolved and after 75 min the reaction mixture was acidified with glacial acetic acid. The solvent was evaporated and the residue was taken up in ethyl acetate. After washing with saturated salt solution, drying, and evaporation of the solvent, 210 mg of crystalline material was obtained. Two recrystallizations from methanol gave 84 mg of analytically pure **8b**: mp 209–212°; $[\alpha]_{589}$ −56°, $[\alpha]_{578}$ −58°, $[\alpha]_{546}$ −66°, $[\alpha]_{436}$ −120°, $[\alpha]_{365}$ −203°; λ_{max} 2.93, 5.76, 7.96 μ; nmr τ 5.05 (m, 3β-H), 5.64 (m, 16-H_2), 6.79 (m, 11β-H), 7.93 (3-OAc).

Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.37; H, 9.24. Found: C, 70.00; H, 9.66.

3α-Acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,14β-androstane-11,17a-dione (10).—A solution of 48 mg of **8b** in 2 ml of acetone was treated with an excess of chromic acid–sulfuric acid reagent.[21] After 5 min at room temperature the excess chromic acid was reduced with methanol and the solution was diluted with water. The solvent was evaporated and the aqueous suspension was extracted with methylene chloride. The methylene chloride solution was washed with saturated salt solution, dried, and evaporated to give 34 mg of material. Recrystallization from methanol gave 20 mg of **10**: mp 214–215°; $[\alpha]_{589}$ −9°, $[\alpha]_{578}$ −9°, $[\alpha]_{546}$ −11°, $[\alpha]_{436}$ −16°, $[\alpha]_{365}$ −3°; λ_{max} 5.70, 5.77, 5.90 μ; nmr τ 5.06 (m, 3β-H), 5.56 and 5.66 (d, J = 4 cps; 16-H_2), 7.92 (3α-OAc).

Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.78; H, 8.74.

3β,11α-Dihydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,14β-androstan-17a-one (9a).—A suspension of 2.00 g of **4b** in 150 ml of absolute ethanol was treated with 1.50 g of sodium borohydride and stirred at room temperature for 4.5 hr. The reaction mixture was acidified with glacial acetic acid and then 5% hydrochloric acid to pH 2, and the solvent was evaporated. The aqueous residue was taken up in methyl isobutyl ketone and washed with saturated salt solution, dried, and evaporated to give 1.761 g of crude **9a**. Recrystallization from methanol gave 561 mg, mp 277–281°. The analytical sample had mp 283–284°; $[\alpha]_{589}$ −37°, $[\alpha]_{578}$ −38°, $[\alpha]_{546}$ −44°, $[\alpha]_{436}$ −82°, $[\alpha]_{365}$ −147°; λ_{max} 2.89, 5.85 μ.

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 72.00; H, 9.60.

3β-Acetoxy-11α-hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,14β-androstan-17a-one (9b).—3β,11α-Dihydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,-14β-androstan-17a-one (**9a**, 300 mg) was dissolved in a mixture of pyridine–acetic anhydride (5.0:2.5) and left overnight at room temperature. After addition of water and evaporation, the residue was recrystallized from methanol to give 176 mg of **9b**, mp 181–184°. Two further recrystallizations gave analytically pure material: mp 197–198°; $[\alpha]_{589}$ −14°, $[\alpha]_{578}$ −14°, $[\alpha]_{546}$ −16°, $[\alpha]_{436}$ −35°, $[\alpha]_{365}$ −74°; λ_{max} 3.00, 5.77 (sh), 5.82, 8.05 (br) μ; nmr τ 5.66 (m, 16-H_2), 6.72 (m, 3α-H), 6.90 (m, 11β-H), 7.95 (3β-OAc).

Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.37; H, 9.24. Found: C, 70.51; H, 9.18.

4α,8,14-Trimethyl-17-oxa-D-homo-18-nor-5α,8α,9β,13α,14β-androstane-3,11,17a-trione (11). A.—An excess of chromic acid–sulfuric acid reagent[21] (10 ml) was added to a solution of 6.95 g of crude isolated reduction product **9a** in 500 ml of acetone under helium and cooled to below 20°. After 10 min the excess chromic acid was reduced with methanol and the reaction mixture was diluted with water. The resulting precipitate was filtered, washed well with water, and dried to give 2.50 g of crude **11**, which on recrystallization from methylene chloride–methanol gave 2.07 g, mp 257–259°. The filtrate was concentrated and extracted with chloroform. The latter phase was washed with saturated salt solution, dried, and evaporated to give an additional 4.20 g of **11**. After recrystallization from methylene chloride–methanol this material weighed 2.12 g, mp 255–257°. The analytical sample had mp 257–260°; $[\alpha]_{589}$ +103°, $[\alpha]_{578}$ +109°, $[\alpha]_{546}$ +112°, $[\alpha]_{436}$ +228°, $[\alpha]_{365}$ +428°; λ_{max} 5.70, 5.89 μ; nmr τ 5.61 (m, 16-H_2).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73; neut equiv, 346. Found: C, 72.94; H, 8.66; neut equiv, 353.

B.—A solution of 81 mg of **8b** in 25 ml of 5% ethanolic potassium hydroxide was left overnight at room temperature. The solution was then acidified with 20% sulfuric acid and diluted with water, and the solvent was evaporated. The aqueous suspension was extracted with ethyl acetate and washed with saturated salt solution, dried, and evaporated to give 73 mg of crude **8a**, mp 237–240°.

Oxidation of 46 mg of this material with chromic acid–sulfuric acid reagent[21] as described above gave 42 mg of crude **11** which on recrystallization from methanol had mp 255–258° and an infrared spectrum (mineral oil) identical with that of the material obtained above.

3α-Hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,-13α,14β-androstane-11,17a-dione (12a).—Two hundred milligrams of **10** was added to 20 ml of a helium-blanketed refluxing solution of 5% ethanolic potassium hydroxide. After 3 hr the solution was acidified with 20% sulfuric acid and diluted with water. The ethanol was evaporated and the aqueous suspension was extracted with methylene chloride. The methylene chloride solution was washed with 5% potassium bicarbonate and saturated salt solution, dried, and evaporated to give 152 mg of **12a** which on recrystallization from methanol gave 44 mg, mp 266–270°. The analytical sample had mp 266–269°; $[\alpha]_{589}$ −179°, $[\alpha]_{578}$ −188°, $[\alpha]_{446}$ −218°, $[\alpha]_{436}$ −401°, $[\alpha]_{365}$ −755°; λ_{max} 2.85, 5.80, 5.87 μ.

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.33; H, 9.33.

The combined mother liquors when taken to dryness had $[\alpha]_D$ −156°.

3α-Acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,-13α,14β-androstane-11,17a-dione (12b).—Room temperature pyridine–acetic anhydride acetylation of **12a** gave **12b**: mp 200–201° (from methanol); $[\alpha]_{589}$ −180°, $[\alpha]_{578}$ −189°, $[\alpha]_{546}$ −218°, $[\alpha]_{436}$ −398°, $[\alpha]_{365}$ −734°; λ_{max} 5.75, 5.80, 5.90 μ; nmr τ 5.09 (m, 3β-H), 5.67 (m, 16-H_2), 7.94 (3α-OAc).

Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.61; H, 8.81.

4α,8,14-Trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androstane-3,11,17a-trione (13).—Compound **11** (342 mg) was added to 35 ml of a helium-blanketed refluxing solution of 5% ethanolic potassium hydroxide. After 3 hr of reflux under helium the solution was acidified to pH 3 with 20% sulfuric acid and diluted with water and the solvent was evaporated. The aqueous residue was extracted with ethyl acetate, washed with water until neutral, dried, and evaporated to give 328 mg of **13**. Recrystallization from methanol gave 210 mg, mp 206–210°, which on further recrystallization gave 138 mg: mp 220–222°; $[\alpha]_{589}$ −153°, $[\alpha]_{578}$ −160°, $[\alpha]_{546}$ −184°, $[\alpha]_{436}$ −329°, $[\alpha]_{365}$ −590°; λ_{max} 5.74, 5.89 μ; nmr τ 5.67 (m, 16-H_2).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73; neut equiv, 346. Found: C, 73.03; H, 8.75; neut equiv, 353.

3β-Acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,-13α,14β-androst-9(11)-en-17a-one (14b).—A solution containing 50 mg of thionyl chloride in 0.5 ml of pyridine was added to 50 mg of **9b** in 1 ml of pyridine cooled to −20°. The reaction mixture was kept at 0° for 30 min and then quenched with water and extracted with ethyl acetate. The ethyl acetate solution was washed with 5% hydrochloric acid and saturated sodium chloride solution, dried, and evaporated to give 43 mg of crude material. Recrystallization from methanol gave 22 mg of **14b**: mp 255–256°; $[\alpha]_{589}$ −30°, $[\alpha]_{578}$ −32°, $[\alpha]_{546}$ −36°, $[\alpha]_{436}$ −63°, $[\alpha]_{365}$ −104°; λ_{max} 5.79, 8.05 μ; nmr τ 4.50 (m, 11-H), 5.66 (m, 16-H_2), 7.94 (3β-OAc).

Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.64; H, 9.12.

Treatment of 14b with Ethanolic Potassium Hydroxide.—Fifty milligrams of **14b** was refluxed with 5 ml of 5% ethanolic potassium hydroxide under the epimerizing conditions described above. After work-up 38 mg of crude 3β-hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androst-9(11)-en-17a-one (**14a**) was obtained. Recrystallization from methanol gave 23 mg of **14a**: mp 231–232°; $[\alpha]_D$ −62°; λ_{max} 3.00, 5.75 μ; nmr τ 4.52 (t, J = 3.5 and 4 cps, 11-H), 5.62 (m, 16-H_2), 5.04 (m, 3α-H).

Reacetylation of this material (pyridine–acetic anhydride, room temperature) and recrystallization gave back 12 mg of **14b**, mp 256–258°, whose infrared spectrum was identical with that of the previously described material.

Ethanolic Potassium Hydroxide Treatment of 9a.—A solution of 50 mg of **9a** in 5 ml of 5% ethanolic potassium hydroxide was refluxed under helium for 3 hr. The reaction was acidified and worked up as described above using methyl isobutyl ketone as the extracting solvent. Recrystallization from methanol gave back 17 mg of **9a**, mp 269–274°, whose infrared spectrum was identical with that of starting material.

3β,17aα-Dihydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androst-9(11)-ene (15a) and 3β-Acetoxy-17aα-hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androst-9(11)-ene (15b).—Sodium borohydride (500 mg in 20 ml of 1:1 dioxane–water) was added to a solution of 500 mg of **14b** in 20 ml of dioxane. The mixture was stirred at room temperature for 17 hr and then glacial acetic acid was added to decompose the excess borohydride. The solution was acidified to pH 2 with 5% hydrochloride acid and the solvent was evaporated. The residue was only partially soluble in ethyl acetate. The insoluble portion (166 mg) on recrystallization from methanol afforded 3β,17aα-dihydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androst-9(11)-ene (**15a**): mp 238–242°; $[\alpha]_{589}$ −36°, $[\alpha]_{578}$ −37°, $[\alpha]_{546}$ −41°, $[\alpha]_{436}$ −63°, $[\alpha]_{365}$ −87° (methanol); λ_{max} 3.10 (br), no absorption 5.0–6.1 μ.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.66; H, 10.41.

The ethyl acetate solution was washed with water until neutral, and the solvent was evaporated to give 365 mg of material melting 180–185°. On repeated recrystallization from methanol, small amounts of the dihydroxy compound **15a** continued to crystallize, mp 234–238°. Concentration of the mother liquors afforded 3β-acetoxy-17aα-hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androst-9(11)-ene (**15b**): mp 190–192°; $[\alpha]_{589}$ −12°, $[\alpha]_{578}$ −15°, $[\alpha]_{546}$ −16°, $[\alpha]_{436}$ −20°, $[\alpha]_{365}$ −21° (methanol); λ_{max} 3.05 (br), 5.77, 8.09 μ; nmr τ 4.56 (t, J = 3 and 3 cps, 11-H), 5.64 (m, 16-H_2), 6.27 (d, J = 7.5 cps, 17a-H), 7.95 (3β-OAc).

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64. Found: C, 72.77; H, 10.06.

3β,17aα-Diacetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androst-9(11)-ene (15c).—The crude mixture from the sodium borohydride reduction of 100 mg of **14b** in 8 ml of dioxane–water (3:1) as described above was dissolved in a mixture of pyridine (2 ml) and acetic anhydride (1 ml) and left overnight at room temperature. Water was added to the reaction mixture and it was evaporated *in vacuo*. Recrystallization of the residue from methanol gave 73 mg of **15c**, mp 95–96°. The analytical sample had mp 98–99°; $[\alpha]_{589}$ −10°, $[\alpha]_{578}$ −11°, $[\alpha]_{546}$ −12°, $[\alpha]_{436}$ −19°, $[\alpha]_{365}$ −21° (methanol); nmr τ 4.58 (t, J = 3.5 and 3.7 cps, 11-H), 5.4–6.2 (complex multiplets, four or five protons), 7.95 (3β-OAc, 17a-OAc).

Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.55; H, 9.24.

3β-Hydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,-13α,14β-androstane-11,17a-dione (17a).—One hundred milligrams of **13** and 100 mg of sodium borohydride were added to 10 ml of 2.5% ethanolic potassium hydroxide solution and stirred at room temperature for 4.5 hr. The excess borohydride was decomposed with glacial acetic acid and the solution was acidified to pH 2 with 5% hydrochloric acid. The solvent was evaporated and the residue was extracted with ethyl acetate, which was washed with saturated sodium chloride solution, dried, and evaporated to give 102 mg of residue. Recrystallization from methanol gave 46 mg of **17a**, mp 252–256°. The analytical sample had mp 255–257°; $[\alpha]_{589}$ −166°, $[\alpha]_{578}$ −174°, $[\alpha]_{546}$ −200°, $[\alpha]_{436}$ −375°, $[\alpha]_{365}$ −715°; λ_{max} 2.95, 5.78, 5.90 μ; nmr τ 5.66 (m, 16-H_2), 6.66 (m, 3α-H).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.53; H, 9.25.

3β-Acetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,-13α,14β-androstane-11,17a-dione (17b).—Pyridine–acetic anhydride acetylation of 51 mg of **17a** at room temperature gave 55 mg of crude **17b**, which after two recrystallizations from methanol gave analytically pure material: mp 287–290° (*in vacuo*); $[\alpha]_{589}$ −131°, $[\alpha]_{578}$ −136°, $[\alpha]_{546}$ −156°, $[\alpha]_{436}$ −295°, $[\alpha]_{365}$ −565°; λ_{max} 5.77, 5.89, 8.05 μ; nmr τ 5.68 (m, 16-H_2), 5.6 (br, 3α-H), 7.94 (3β-OAc).

Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.67; H, 8.73.

3β,17aα-Dihydroxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androstan-11-one (18a).—A solution of 100 mg of **13** and 100 mg of sodium borohydride in 10 ml of absolute ethanol was stirred at room temperature for 4 hr. After decomposition of the excess hydride with glacial acetic acid, the pH was adjusted to 2 with 5% hydrochloric acid and the solvent was evaporated. The aqueous residue was extracted with ethyl acetate, which was washed until neutral, dried, and evaporated. Crystallization of the residue from acetone–hexane gave **18a**, mp 242–245°. The analytical sample had mp 246–248°; $[\alpha]_{579}$ −158°, $[\alpha]_{578}$ −165°, $[\alpha]_{546}$ −213°, $[\alpha]_{436}$ −339°, $[\alpha]_{365}$ −624°; λ_{max} 2.83 (sh), 3.00, 5.93 μ.

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 72.03; H, 9.89.

3β,17aα-Diacetoxy-4α,8,14-trimethyl-17-oxa-D-homo-18-nor-5α,8α,13α,14β-androstan-11-one (18b).—Acetylation of 155 mg of **18a** was carried out in the usual manner (pyridine–acetic anhydride, room temperature) to give after crystallization from methanol 54 mg of **18b**, mp 194–197°. Further recrystallization raised the melting point to 208–209°; $[\alpha]_{589}$ −94°, $[\alpha]_{578}$ −98°, $[\alpha]_{546}$ −111°, $[\alpha]_{436}$ −204°, $[\alpha]_{365}$ −388°, $[\alpha]_D$ −84° (methanol); λ_{max} 5.70 (sh), 5.79, 5.92, 8.06 μ; nmr τ 4.41 (d, J = 7.5 cps, 17a-H), 5.61 (m, 16-H_2), 6.16 (m, 3α-H), 7.91, 7.94 (17a-OAc, 3β-OAc).

Anal. Calcd for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81. Found: C, 69.16; H, 8.82.

Acetylation of the mother liquors of **18a** from the sodium borohydride–ethanol reduction of **13** gave 34 mg of high-melting (249–252°) material which on further recrystallization from methanol gave 5 mg of **17b**, mp 282–285° *in vacuo*.

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