**$\Delta^{7,9(11)}$-22-Isoallospirostadiene-3$\beta$-ol Acetate (X).**—A thoroughly dried sample of VIIIa (262 mg.) was dissolved in 1.9 cc. of anhydrous pyridine, chilled to 0°, and treated with 0.2 cc. of redistilled thionyl chloride. The reaction mixture was allowed to stand at 0–5° for 16 hours. At the end of this period the reaction mixture was allowed to come to room temperature and then rechilled and decomposed with ice-water. The decomposed reaction mixture was extracted with ether and the ether solution of the product washed successively with dilute hydrochloric acid, 5% aqueous sodium bicarbonate and water. Evaporation of the dried ether solution gave 0.280 g. of amorphous solid which gave a strong test for unsaturation (yellow color) with tetranitromethane and showed only very weak absorption in the 240–250 m$\mu$ region. This material was dissolved in petroleum ether–benzene (7:1) and passed through a short column of alumina to give after recrystallization from ethyl acetate 0.076 g. of X, m.p. 205–213.5°, $\lambda_{max}$ 2350 Å., log $\epsilon$ 4.14, $\lambda_{max}$ 2420 Å., log $\epsilon$ 4.19, and $\lambda_{max}$ 2500 Å., log $\epsilon$ 4.0 (methanol).

*Anal.* Calcd. for $C_{29}H_{42}O_4$: C, 76.61; H, 9.31. Found: C, 77.00; H, 9.40.

A mixed melting point of this material with an authentic sample of X[13] showed no depression and the infrared spectra of the two samples were identical.

A second crop of X amounting to 0.056 g., m.p. 203–210°, brought the over-all yield on the conversion VIII → X to 60%.

RAHWAY, N. J.

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[JOINT CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA, AND THE RESEARCH LABORATORIES OF MERCK AND CO., INC.]

# The Preparation of $\Delta^{5,7}$-Steroidal Dienes[1]

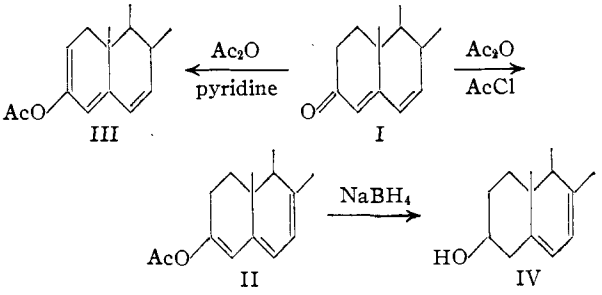
BY W. G. DAUBEN, J. F. EASTHAM, R. A. MICHELI, K. H. TAKEMURA, L. MANDELL AND J. M. CHEMERDA

RECEIVED DECEMBER 17, 1952

When $\Delta^{4,6}$-cholestadiene-3-one or $\Delta^{4,6}$-22-isospirostadiene-3-one was allowed to react with acetyl chloride and acetic anhydride, the 3-acetoxy-$\Delta^{3,5,7}$-trienes were formed. If the isospirostadienone reaction was conducted in the presence of one equivalent of pyridine, the side chain was opened and 3,26-diacetoxy-$\Delta^{3,5,7,20(22)}$-furostetraene was obtained. When the acetylation of either ketone was performed in the presence of excess pyridine and acetic anhydride or with isopropenyl acetate and acid, the isomeric 3-acetoxy-$\Delta^{2,4,6}$-trienes were formed. Reduction of the 3-acetoxy-$\Delta^{3,5,7}$-trienes with sodium borohydride yielded the $\Delta^{5,7}$-diene-3-ols. A discussion of the possible mechanisms of these enolizations is given. Comparison of the molecular rotations in these series suggest a vicinal effect.

The conversion of $\Delta^5$-steroids to $\Delta^{5,7}$-steroid dienes has become of importance due to the recent work which has shown that such dienes are useful starting substances for the introduction of an 11-oxygen function into the steroid nucleus.[2] Several methods are available for the introduction of such unsaturation and all involve the preparation of a 7-substituted-$\Delta^5$-sterol with subsequent elimination of the elements of water or acid from the 7,8-position.[3] A synthetic sequence not involving the preparation of a 7-substituted steroid appeared to warrant investigation.

It has previously been reported[4] that when the enol acetate of cholestenone (3-acetoxy-$\Delta^{3,5}$-cholestadiene) is allowed to react with sodium borohydride, the product is the $\beta,\gamma$-unsaturated alcohol, cholesterol. The mechanism of such a reduction has been shown to proceed through the 3-keto-$\Delta^5$-steroid,[4,5] reduction occurring prior to the migration of the unsaturated center to a position of conjugation. Thus, if the enol acetate of a steroid containing the desired $\Delta^{5,7}$-system could be prepared from the easily available intermediate, $\Delta^{4,6}$-3-keto steroid, it should serve as a source of the $\Delta^{5,7}$-steroidal dienes. Such an enol acetate has been prepared in the ergosterol series by Heilbron and his co-workers[6] and in the sapogenin series by Yashin, Rosenkranz and Djerassi[7] but in both cases the source of their enol esters was the desired 3-hydroxy-$\Delta^{5,7}$-compound itself.




It has now been found that when $\Delta^{4,6}$-cholestadien-3-one (I), easily prepared from cholesterol[8] using the Wettstein modification[9] of the Oppenauer oxidation employing quinone and aluminum isopropoxide, is allowed to react with a mixture of acetyl chloride and acetic anhydride, 3-acetoxy-$\Delta^{3,5,7}$-cholestatriene (II) is the sole product obtained in pure form. The spectroscopic properties of the product were in good agreement with those

(1) A preliminary announcement of part of this work was reported in THIS JOURNAL, **73**, 4496 (1951).

(2) E. M. Chamberlin, W. V. Ruyle, A. E. Erickson, J. M. Chemerda, L. M. Aliminosa, R. L. Erickson, G. E. Sita and M. Tishler, THIS JOURNAL, **73**, 2396 (1951); L. F. Fieser, J. E. Herz and Wei-Yuan Huang, *ibid.*, **73**, 2397 (1951); H. Heusser, K. Eichenberger, P. Kurath, H. R. Dallenbach and O. Jeger, *Helv. Chim. Acta*, **34**, 2106 (1951); R. C. Anderson, R. Budziarck, G. T. Newbold, R. Stevenson and F. S. Spring, *Chemistry and Industry*, 1035 (1950); G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 3456 (1951).

(3) For leading references see v. J. Schmutz, H. Schaltegger and M. Sanz, *Helv. Chim. Acta*, **34**, 1111 (1951); and L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., 1949, pp. 179–182.

(4) E. Schwenk, M. Gutand and J. Belisle, *Arch. Biochem. Biophys.*, **31**, 456 (1951); T. F. Gallagher and B. Belleau, THIS JOURNAL, **73**, 4458 (1951); W. G. Dauben and J. F. Eastham, *ibid.*, **73**, 4463 (1951).

(5) W. G. Dauben, R. A. Micheli and J. F. Eastham, *ibid.*, **74**, 3582 (1952).

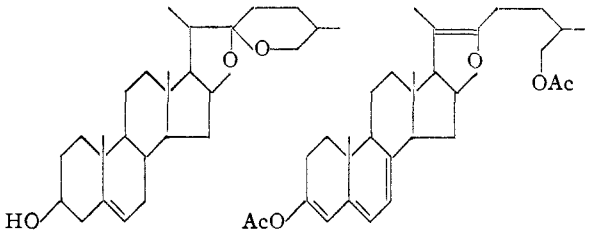
(6) I. M. Heilbron, T. Kennedy, F. S. Spring and G. Swain, *J. Chem. Soc.*, 869 (1938).

(7) R. Yashin, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 4654 (1951).

(8) A. L. Wilds and C. Djerassi, *ibid.*, **68**, 1712 (1946), and earlier references.

(9) A. Wettstein, *Helv. Chim. Acta*, **23**, 388 (1940).

reported for similar compounds in other series.[6,7] No evidence for the presence of the $\Delta^{2,4,6}$-isomer could be found either by investigation of the mother liquors or by spectroscopic examination of the reaction mixture. When the pure material II was reduced with sodium borohydride and the reaction mixture separated by digitonin, crude 7-dehydrocholesterol (IV) was obtained in 75% yield. The sterol was purified through its 3,5-dinitrobenzoate. When crude enol acetate obtained directly from the reaction mixture was reduced, the over-all yield from dienone was about 35%.

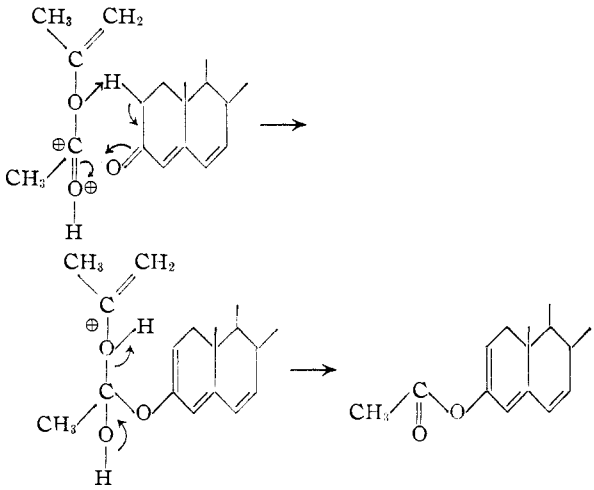



VIII V

This method was also investigated using diosgenin (V). This sapogenin was oxidized, as above, to $\Delta^{4,6}$-22-isospirostadiene-3-one (VI); this transformation had been carried out previously by Marker and Turner[10] in 30% yield but by utilizing a modification in their work-up procedure (see Experimental) it was found possible to increase the yield to 50–55%. When the dienone VI was allowed to react with acetic anhydride and acetyl chloride the 3-acetoxy-$\Delta^{3,5,7}$-22-isospirostatriene (VII) was obtained and was identical with that previously prepared from $\Delta^{4,7}$-22-isospirostadien-3-one.[7] This preparation was complicated, in part, by the tendency of the starting ketone to form 3,26-diacetoxy-$\Delta^{3,5,7,20(22)}$-furostetraene (VIII). When the enol acetylation was conducted with the same reagents in the presence of *one equivalent* of pyridine, the enol acetate of furostetraene (VIII) was formed in 40% yield. This facile cleavage of the side chain to the furostene is somewhat anomalous for acetyl chloride and acetic anhydride under catalysis by hydrogen chloride, while effecting enolization of the dienone (VI) to 3-chloro-$\Delta^{3,5,7}$-22-isospirostatriene (IX), left the side chain intact.

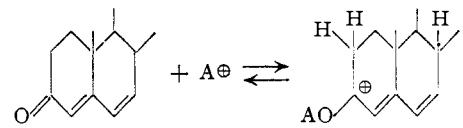
Sodium borohydride reduction of 3-acetoxy-$\Delta^{3,5,7}$-22-isospirostatriene (VII) has not been studied thoroughly since, after preliminary experiments had been performed and results similar to those in the cholesterol series had been obtained, Ringold, Rosenkranz and Djerassi[11] published a detailed study of the reduction of the same trienol acetate (prepared from $\Delta^{4,7}$-dien-3-one).

When either of the $\Delta^{4,6}$-dien-3-ones (I or VI) were heated with excess pyridine and acetic anhydride or with isopropenyl acetate with acid catalysis, the 3-acetoxy-$\Delta^{2,4,6}$-trienes of type III were formed. The spectral properties of these compounds were in agreement with those reported for a similar compound in the ergosterol series.[6] It is apparent that in the enol acetylation reaction, the $\Delta^{3,5,7}$-triene system is formed under acid conditions (with exception of the acid-catalyzed isopropenyl acetate reaction[12]) and the $\Delta^{2,4,6}$-system under basic conditions.



There are two possible interpretations of such results. First, it could be assumed that the $\Delta^{2,4,6}$-trienic system is formed more rapidly under both sets of conditions, but that under acidic conditions equilibration to a more stable $\Delta^{3,5,7}$-triene is possible. However, from ultraviolet analysis on total crude reaction mixtures, this mechanism appears unlikely for in no experiment were mixtures of the two trienes detected. Furthermore, conversion of the $\Delta^{2,4,6}$-triene to the $\Delta^{3,5,7}$-triene, or mixtures thereof, under acid catalysis could not be demonstrated and, in fact, in the acid-catalyzed isopropenyl acetate acetylation the $\Delta^{2,4,6}$-system is formed and appears stable.

A more likely reaction path appears to be that under acid catalysis the initial step is the coordination of an acid fragment (such as $CH_3CO^{\oplus}$ or its equivalent represented by $A^{\oplus}$) with the $C_3$ carbonyl group. The rationalization for the loss of



the proton at $C_8$ in preference to the more accessible protons at $C_2$ in order to satisfy the carbonium ion at $C_3$ might involve the same considerations as those previously advanced for the "Saytzeff Rule" for the dehydrohalogenation of alkyl halides.[13,14] Thus, the transition state for the $\Delta^{3,5,7}$-triene can be stabilized to a greater extent by hyperconjugation than the corresponding transition state for the $\Delta^{2,4,6}$-triene.[15] The formation of the $\Delta^{2,4,6}$-triene,

(10) R. E. Marker and D. L. Turner, THIS JOURNAL, **63**, 767 (1941).

(11) H. J. Ringold, G. Rosenkranz and C. Djerassi, *ibid.*, **74**, 3441 (1952).

(12) The anomalous action of isopropenyl acetate and acid catalysis to yield a $\Delta^{2,4,6}$-triene (the same product as obtained under basic conditions with other reagents) may be rationalized if one assumes that isopropenyl acetate functions as an internal base and thereby alters the usual course of the acid-catalyzed reaction.

(13) C. K. Ingold, *Trans. Faraday Soc.*, **37**, 674 (1941).

(14) M. L. Dhan, E. D. Hughes, C. K. Ingold, A. M. M. Mandour, G. A. Maw and L. I. Wolff, *J. Chem. Soc.*, 2093 (1948).

(15) For other discussions of the role of hyperconjugation in the stabilization of enols and polyene systems, see H. M. E. Cardwell and A. E. H. Kilmer, *J. Chem. Soc.*, 2430 (1951); H. M. E. Cardwell, *ibid.*, 2442 (1951); D. H. R. Barton, *ibid.*, 257 (1951).

however, would be favored in basic media since the less hindered $C_2$ proton can be more readily attacked by the base and thus generate the enolate of the $\Delta^{2,4,6}$-triene which would then be acetylated.

These concepts can be extended to explain the enol acetylation of 20-keto steroids. It has been reported that with acetic anhydride and acid catalysis[16] the $\Delta^{17(20)}$-enol acetate is formed while with isopropenyl acetate and acid catalysis[17] the $\Delta^{20(21)}$-enol is obtained. The formation of $\Delta^{17(20)}$-isomers would be expected under acid conditions considering the hyperconjugative effect on the $\Delta^{17(20)}$-transition state. With isopropenyl acetate, if the "internal base" type mechanism postulated above operates, the less hindered $C_{21}$ proton would be lost and lead to the formation of the $\Delta^{20(21)}$-enol acetate.

It is of interest to compare the optical rotations of the compounds in this series and the molecular rotation differences are given in Table I. In this table where comparison is made in each series, it is seen that the structural changes produce optical anomalies and thus do not allow for the method of molecular rotation difference[18] to be applied to correlate structures of compounds in these different series. It is, however, of interest to note the unusually high positive rotation for $\Delta^{4,6}$-cholestane-3-one ($M_D$ + 126), the large negative rotation for the $\Delta^{4,7}$-22-isospirostadiene-3-one ($M_D$ − 266) and the large difference between the isomeric enol acetates in the cholestane series.

TABLE I

MOLECULAR ROTATION DIFFERENCES

| Compound | $\Delta M_D$ from parent $\Delta^{4,6}$-diene-3-one[d] Cholestane | Ergostane | Iso-spirostane |
|---|---|---|---|
| $\Delta^{4,7}$-Diene-3-one | +4[a] | + 98[b] | − 40[c] |
| 3-Acetoxy-$\Delta^{3,5,7}$-triene | −961 | −507[b] | −509[c] |
| 3-Acetoxy-$\Delta^{3,4,6}$-triene | −204 | −252[b] | −244 |

[a] For rotation see A. Windaus and O. Kaufmann, *Ann.*, **542**, 218 (1939). [b] See reference 6. [c] See reference 7. [d] For parent dienones see references 8, 6 and J. Romo, H. J. Ringold, G. Rosenkranz and C. Djerassi, *J. Org. Chem.*, 16, 1873 (1951).

## Experimental

**3-Acetoxy-$\Delta^{3,5,7}$-cholestatriene** (II).—A solution of 3.0 g. (7.87 mmoles) of $\Delta^{4,6}$-cholestadiene-3-one[8] in 15 ml. of purified acetic anhydride[20] and 3 ml. of purified acetyl chloride[19] was heated in the dark on a steam-bath for 18 hours. The entire apparatus employed was scrupulously dried and the reaction conducted under nitrogen. The resulting tan solution, while still warm, was poured slowly with stirring into 35 ml. of C.P. methanol cooled in an ice–salt bath. The flask was rinsed with acetic anhydride. After cooling the resulting solid for one hour in a refrigerator, the material was filtered and washed with ice-cold methanol, yield 1.91 g. (57.3%).[20] Two recrystallizations from ether–methanol yielded 0.82 g. (24.6%), m.p. 101–102°[21]; ultraviolet, $\lambda_{max}^{ethanol}$ 303 mμ (ε 16,200); 315 mμ (ε 22,100); 329 mμ (ε 15,700)[22]; $[\alpha]^{25}D$ −149.3° (*c* 0.288 in $CHCl_3$, α −0.430).

*Anal.* Calcd. for $C_{29}H_{44}O_2$ (424.64): C, 82.02; H, 10.44. Found: C, 81.88; H, 10.22.

**Reduction of 3-Acetoxy-$\Delta^{3,5,7}$-cholestatriene** (II).—The trienol acetate (0.210 g., 0.495 mmole) was dissolved in 20 ml. of dry ether and 35 ml. of C.P. methanol. To this solution there was added in one portion a solution of 0.350 g. of sodium borohydride in 3 ml. of water and 10 ml. of methanol. The reaction mixture was flushed with nitrogen, the flask closed and the solution stirred for 3.5 hours at room temperature in the dark. After dilution with water and extraction with ether, the ethereal solution was washed with water and dried over sodium sulfate. Evaporation of the solvent at room temperature and drying of the residue overnight under reduced pressure yielded 191 mg. of crude dienols.

The solid was dissolved in 15 ml. of 90% ethanol and to this there was added a solution of 610 mg. of digitonin in 20 ml. of ethanol. After standing at 0° for 12 hours, the mixture was filtered and 632 mg. (76.3% β) of the digitonide was obtained. The digitonide was dissolved in pyridine and the sterol precipitated with ether in the usual manner, yield 140 mg. (73.7% based upon enol acetate) of crude 7-dehydrocholesterol.

The crude sterol was dissolved in 0.5 ml. of dry pyridine and 300 mg. of freshly-prepared 3,5-dinitrobenzoyl chloride was added. The mixture was heated on a steam-bath for one hour, diluted with sodium bicarbonate solution and the solid filtered. The crude ester was refluxed with 8 ml. of acetone for 5 minutes, the solution cooled to 0°, filtered and dried. The yellow-orange needles weighed 120 mg. (42% based upon enol acetate), m.p. 206.3–207.0°, no depression upon admixture with an authentic sample.[23]

When 100 mg. of the enol acetate was reduced and the isomers separated as above, 75 mg. of crude 7-dehydrocholesterol was obtained. After recrystallization from ether–methanol, it melts from 142–143° (lit.[24] 142–143.5°), $[\alpha]^{25}D$ −115° (lit.[24] −113.6°).

When 500 mg. of the dienone was converted to the enol acetate as described above and the material not recrystallized but reduced directly, 500 mg. of reduction product was obtained. Without separation of the isomers with digitonin, the mixed sterols were converted to the benzoate esters and the esters recrystallized, yield 230 mg. (37% based on dienone), m.p. 126–129°, $[\alpha]^{25}D$ −48.7°. This material was practically pure β-isomer since Windaus and Naggatz[25] report the following properties for the benzoates: β-benzoate, m.p. 139–140°, $[\alpha]^{25}D$ −53.2°; α-benzoate, m.p. 118–119°, $[\alpha]^{25}D$ +48.5°.

**3-Acetoxy-$\Delta^{2,4,6}$-cholestatriene** (III).—A solution of 1.0 g. of $\Delta^{4,6}$-cholestadiene-3-one, 0.1 g. of *p*-toluenesulfonic acid monohydrate in 40 ml. of benzene was heated to distil 20 ml. of the benzene. Isopropenyl acetate (10 ml.) was added and the solution refluxed for four hours under a nitrogen atmosphere with the exclusion of light. After cooling, 60 mg. of anhydrous sodium acetate was added and the mixture concentrated under reduced pressure at 45°. The residual material was dissolved in ether and the ethereal solution washed successively with dilute sodium bicarbonate, water and saturated sodium chloride and finally dried over

(16) C. W. Marshall, T. H. Kritchevsky, S. Lieberman and T. F. Gallagher, THIS JOURNAL, **70**, 1837 (1948).

(17) R. B. Moffett and D. I. Weisblat, *ibid.*, **74**, 2183 (1952); H. Vanderhaeghe, E. R. Katzenellenbogen, K. Dobriner and T. F. Gallagher, *ibid.*, **74**, 2810 (1952).

(18) For a complete discussion with the pertinent references see footnote 3, L. F. Fieser and M. Fieser, pp. 204–219.

(19) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1941, p. 380.

(20) The low intensity in the 280 mμ region of the spectrum of this crude product showed the almost complete absence of the starting ketone.

(21) After completion of this work, R. Antonucci, S. Bernstein, M. Heller and J. H. Williams (*J. Org. Chem.*, **17**, 1446 (1952)) reported similar properties for this compound prepared from $\Delta^{4,7}$-cholestadiene-3-one.

(22) In the original communication,[1] the properties reported for an analytically pure product were: m.p. 91–93°, $[\alpha]^{25}D$ −69° and $\lambda_{max}^{ethanol}$ 316 mμ (ε 20,800). Since finding the higher values reported above, we have repeated our original work and find that after one recrystallization an analytically pure product with these low properties can be obtained and further recrystallization raises the values. An examination of the mother liquors from the recrystallizations was indecisive since only oils could be obtained and the spectrum of the oil was quite similar to that of the starting dienone. At present, we have no indication as to the nature of the impurity in our original material. The ultraviolet spectrum of the crude reaction product does not rule out the isomeric enol acetate, but as shown in later experiments, it does not seem likely.

(23) Kindly supplied by E. I. du Pont de Nemours and Co., Inc.

(24) A. Windaus, H. Lettre and Fr. Schench, *Ann.*, **520**, 98 (1936).

(25) A. Windaus and J. Naggatz, *ibid.*, **542**, 204 (1939).

sodium sulfate. The ether was removed (water-bath 40–50°) and the residue recrystallized from methanol, yield 0.95 g. (85%), pale yellow crystals, m.p. 100–103°. After recrystallization several times from ether–methanol, the white crystals melt 101–103.5° (immersed at 100°, turbid melt at 102.2°, clear melt at 103.5°), $[\alpha]^{25}D$ −18.5° ($CHCl_3$); $\lambda_{max}^{ethanol}$ 302 mμ, ε 12,700.

*Anal.* Calcd. for $C_{29}H_{44}O_2$ (424.64): C, 82.02; H, 10.44. Found: C, 82.18; H, 10.62.

**$\Delta^{4,6}$-22-Isospirostadiene-3-one (VI).**—A solution of 50 g. of diosgenin and 300 g. of benzoquinone in 3500 ml. of dry toluene was heated and 100 ml. of toluene allowed to distil. At this time, 101 g. of aluminum *t*-butoxide was added and the solution refluxed for 1.5 hours. The majority of the toluene (2400 ml.) was removed under reduced pressure and the residue steam-distilled until no toluene appeared in the distillate. To the black residue, cooled in an ice-bath, there was added 1200 ml. of cold 1 *N* sulfuric acid and this mixture extracted with 3 one-liter portions of ether. The ether extract was washed twice with 500-g. portions of 1 *N* sulfuric acid and twice with one-liter portions of water. Aqueous 5% sodium hydroxide was added in liter portions, *without shaking*, and separated and this process repeated until the color of the ethereal solution no longer lightened. Finally the ether solution was washed thoroughly with one liter of 5% sodium hydroxide, one liter of water, dried over sodium sulfate and the ether removed. The residue was dissolved in 250 ml. of ether and chromatographed on 1 kg. of acid washed alumina. From the ether eluate (5 l. ether) 24 g. of $\Delta^{4,6}$-22-isospirostadiene-3-one was obtained, m.p. 208–210°; $\lambda_{max}^{methanol}$ 284 mμ (ε 18,600).

It was subsequently found that if the benzoquinone was recrystallized from methanol before use, the ketone may be purified by direct recrystallization.

**3-Acetoxy-$\Delta^{3,5,7}$-22-isospirostatriene (VII).**—$\Delta^{4,6}$-22-Isospirostadiene-3-one (0.5 g.) dissolved in a mixture of 2.5 ml. of purified acetic anhydride and 0.5 ml. of purified acetyl chloride was heated for 16 hours on the steam-bath under an atmosphere of nitrogen and protected from light. The excess solvent was removed under high vacuum and the ultraviolet spectrum run on a solution of the crude product in methanol. The results were an inflection at 289 mμ (ε 7,760), maxima at 300 mμ (ε 11,500), 314 mμ (ε 11,750) and 328 mμ (ε 8,700).

Alternately, the reaction mixture was poured into 8 ml. of cold methanol with stirring. The crystalline material was filtered, dissolved in the minimum volume of boiling ether and the ether displaced with boiling methanol. The crystalline trienol acetate melts 187–190° (lit.[7] 188–190°), yield 100 mg. (18.2%); $\lambda_{max}^{methanol}$ 302 mμ (ε 15,800), 314 mμ (ε 17,800) and 329 mμ (ε 15,100).[26]

**3-Chloro-$\Delta^{3,5,7}$-22-isospirostatriene (IX).**—A solution of 3.0 g. of $\Delta^{4,6}$-22-isospirostadiene-3-one in a mixture of 21 ml. of acetyl chloride and 12 ml. of acetic anhydride, into which had previously been passed a steady stream of dry hydrogen chloride for 10 minutes, was refluxed for 5 hours. The solvents were removed under reduced pressure and the residue dissolved in ether, washed with cold 5% sodium bicarbonate and then water. The ethereal solution was dried over sodium sulfate, concentrated under reduced pressure and chromatographed on 60 g. of acid-washed alumina. From the petroleum ether eluate, 1.25 g. of 3-chloro-$\Delta^{3,5,7}$-22-isospirostatriene was obtained which was recrystallized from benzene–methanol, yield 1.1 g. (35.1%), m.p. 156–157.5°; $\lambda_{max}^{methanol}$ 305 mμ (ε 19,100), 318 mμ (ε 25,100) and 334 mμ (ε 17,800). The infrared spectrum indicated no carbonyl and no hydroxyl groups and an intact side chain.[27]

*Anal.* Calcd. for $C_{27}H_{37}O_2Cl$ (429.03): C, 75.58; H, 8.69; Cl, 9.26. Found: C, 75.12; H, 8.69; Cl, 9.14.

**3,26-Diacetoxy-$\Delta^{3,5,7,20(22)}$-furostetetraene (VIII).**—Pyridine (0.1 ml., one mole per mole of sapogenin) was added to 0.5 ml. of acetyl chloride and 2.5 ml. of acetic anhydride. To this mixture was added 0.5 g. of $\Delta^{4,6}$-22-isospirostadiene-3-one and the solution refluxed for three hours. The solvent was removed under high vacuum and the residue triturated with methanol. The solid was filtered and recrystallized from methanol, yield 0.25 g. (41.4%), m.p. 101–103°; $\lambda_{max}^{methanol}$ 301 mμ (ε 18,600), 314 mμ (ε 22,400) and 329 mμ (ε 16,600). The infrared spectrum shows the side-chain is not intact and the presence of an isolated double bond, 6.01 μ.

*Anal.* Calcd. for $C_{31}H_{42}O_5$ (494.64): C, 75.27; H, 8.56. Found: C, 75.52; H, 8.39.

**3-Acetoxy-$\Delta^{2,4,6}$-22-isospirostatriene.**—A solution of 3.0 g. of $\Delta^{4,6}$-22-isospirostadiene-3-one and 0.3 g. of *p*-toluenesulfonic acid in 120 ml. of benzene was heated and 60 ml. of benzene distilled. To this solution was added 30 ml. of isopropenyl acetate and the mixture refluxed for 4 hours. The solvent was removed under reduced pressure and the residue dissolved in ether. The ethereal solution was washed with 5% sodium bicarbonate, water, dried over sodium sulfate and the solution concentrated to dryness. The residue was recrystallized from benzene–methanol, yield 3.0 g. (90.6%), m.p. 166–169°, $[\alpha]^{25}D$ −104°; $\lambda_{max}^{methanol}$ 302 mμ (ε 14,800). The presence of bands in the infrared spectrum at 10.2 and 11.1 μ indicates an intact side chain.

*Anal.* Calcd. for $C_{29}H_{38}O_4$ (450.59): C, 76.95; H, 8.91. Found: C, 76.26; H, 8.50.

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(26) By combining the curves of pure $\Delta^{3,5,7}$-trienol acetate and $\Delta^{4,6}$-diene-3-one, all absorption in the spectrum of the total crude product could be accounted for and thus indicating no isomeric $\Delta^{2,4,6}$-trienol acetate was present. This type of analysis was made on all total crude products in the enolization experiments and in *no* case were mixtures of the two enol acetates found.

(27) It has been observed in these laboratories (Merck) that two bands at 10.2μ and 11.1μ are associated with the diosgenin side chain.