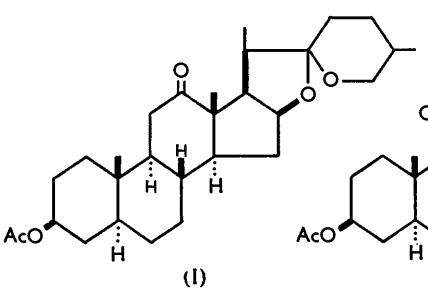
835. *Studies in the Synthesis of Cortisone. Part XV.* Improvements in the Conversion of Hecogenin into 3β : 12β-Diacetoxy-5α : 25D-spirostan-11-one † and a Study of the Isomeric 11 : 12-Ketols.‡*

By J. Elks, G. H. Phillipps, T. Walker, and L. J. Wyman.

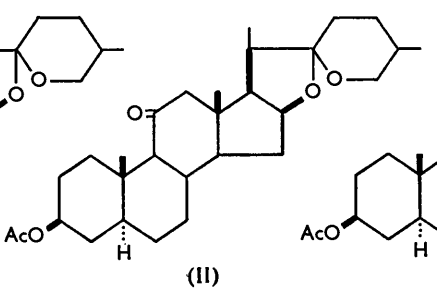
Study of the conversion of hecogenin acetate into 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one *via* 11 : 23-dibromohecogenin acetate has made possible an overall yield of 77%.

Some other 11 : 12-ketols of the spirostan series have been prepared and certain of their reactions examined.

The occurrence of hecogenin in the waste-products from sisal manufacture [1] makes it an attractive starting material for the synthesis of cortisone and related steroid hormones, and methods have been described for converting hecogenin acetate (I) into 11-oxotigogenin acetate (II) [2,3,4] and 3β-acetoxy-5α : 25*D*-spirosta-7 : 9(11)-dien † (III),[5] both of which



(I)



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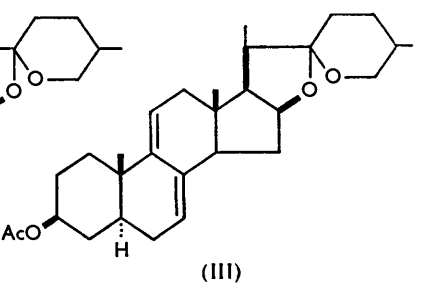


(III)

have in turn been converted into cortisone.[6,7] However, all of these methods leave something to be desired in yield and the number of stages.

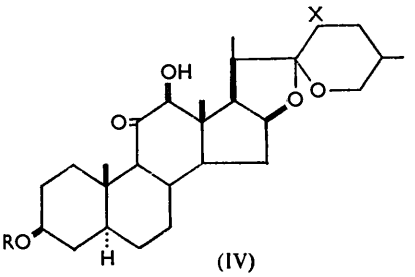
The method used in the bile-acid series by Borgstrom and Gallagher [8,9] for transferring an oxygen atom from $C_{(12)}$ to $C_{(11)}$ involves replacement of the 12β-hydroxy-group in a 12β-hydroxy-11-ketone by bromine, and it cannot be applied to 3-monoesters (IV; X = H) of 3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one because the spirostan side-chain is

* Part XIV, preceding paper. † The term "25*D*-spirostan" is used, in this and the following paper, to mean the same configuration at $C_{(20)}$, $C_{(22)}$, and $C_{(25)}$ as that of the naturally occurring "*iso*-sapogenins." It is, therefore, synonymous with the older, but now untenable, term "22*a*-spirostan."

‡ Submitted in honour of the seventieth birthday of Sir Ian Heilbron, D.S.O., F.R.S.

[1] Callow, Cornforth, and Spensley, *Chem. and Ind.*, 1951, 699; Spensley, *ibid.*, 1952, 426.
[2] Cornforth, Osbond, and Phillipps, *J.*, 1954, 907.
[3] Schmidlin and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 1241.
[4] Djerassi, Ringold, and Rosenkranz, *J. Amer. Chem. Soc.*, 1954, **76**, 5533.
[5] Hirschmann, Snoddy, and Wendler, *ibid.*, 1953, **75**, 3252.
[6] Rosenkranz and Sondheimer, *Fortschr. Chem. org. Naturstoffe*, 1953, **10**, 274.
[7] (*a*) Cameron, Evans, Hamlet, Hunt, Jones, and Long, *J.*, 1955, 2807; (*b*) Barton, Evans, Hamlet, Jones, and Walker, *J.* 1954, 747; (*c*) Chamberlin and Chemerda, *J. Amer. Chem. Soc.*, 1955, **77**, 1221; (*d*) Evans, Hamlet, Hunt, Jones, Long, Oughton, Stephenson, Walker, and Wilson, *J.*, 1956, 4356.
[8] Borgstrom and Gallagher, *J. Biol. Chem.*, 1949, **177**, 951.
[9] Hershberg, Herzog, Coan, Weber, and Jevnik, *J. Amer. Chem. Soc.*, 1952, **74**, 2585.

attacked by phosphorus tribromide.[4,10] The corresponding *allo*pregnan-20-ones (V; R = H and Ac) have been prepared from (IV; X = H),[10,11,12] but there is no report of the removal of the 12β-substituents from them.



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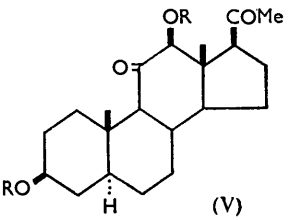
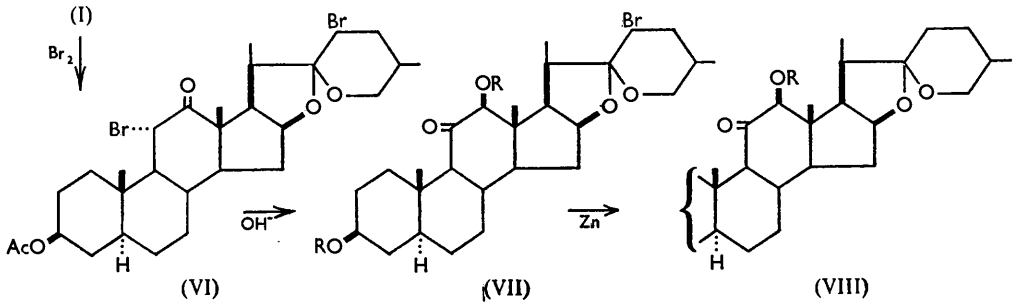


(V)

In the search for a more convenient method of passing from hecogenin acetate (I) to the 11-oxo-compound (II), we have re-investigated both the preparation and the reduction of 3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one (VIII; R = H) and its derivatives. The successful outcome of the second of these studies is described in the next paper; we deal here with improvements in the preparation of the ketone (VIII) and with certain related topics.

Hecogenin acetate (I) has been converted into 3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one (VIII; R = H) by bromination, treatment of the resulting 11 : 23-dibromo-compound with alkali, and removal of the alkali-stable 23-bromine atom with zinc,[9,10] but the yields were not very high. For our initial experiments we prepared the pure 11α : 23-dibromo-compound (VI). Bromination of hecogenin acetate in chloroform [2,5] led to rather erratic results, and we found dioxan, carbon tetrachloride, or benzene more satisfactory.



From a bromination in carbon tetrachloride a small yield of an isomeric dibromohecogenin acetate was also isolated which, for the following reasons, we believe to be the $C_{(23)}$-isomer of the known compound (VI): (*a*) hecogenin acetate was regenerated by treatment with zinc, (*b*) the carbonyl band in the infrared spectrum suggested the presence of the equatorial 11α-bromine atom,[13,14] and the absorption in the 800—1100 cm.$^{-1}$ region (characteristic of the spiroketal system) differed from that of both compounds (I) and (VI),[13] (*c*) dehydrobromination with collidine gave a bromo-9(11)-dehydrohecogenin acetate ($\lambda_{max.}$ 237·5 mμ), which differed from that obtained in a similar way from the dibromide (VI), but agreed in its properties with the " 23*b*-bromo-9(11)-dehydrohecogenin acetate " described by Mueller and Norton.[15] It should be said that there is no evidence positively ruling out the possibility that the bromo-compounds of the new series have the bromine atom at $C_{(20)}$, but we propose nevertheless to adopt Mueller and Norton's convention.

[10] Mueller, Norton, Stobaugh, Lin Tsai, and Winniford, *J. Amer. Chem. Soc.*, 1953, **75**, 4892.
[11] Djerassi, Martinez, and Rosenkranz, *J. Org. Chem.*, 1951, **16**, 303.
[12] Martinez, Ringold, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1953, **75**, 239.
[13] Dickson and Page, *J.*, 1955, 447.
[14] Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[15] Mueller and Norton, *ibid.*, p. 749.

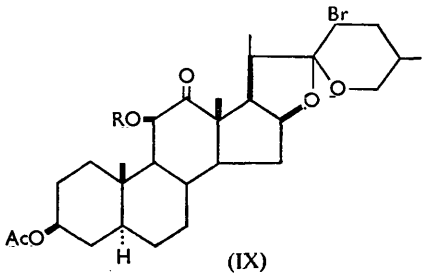
Treatment of 11α : 23*a*-dibromohecogenin acetate (VI) with methanolic potassium hydroxide under the conditions used by Djerassi *et al.*[11] gave a crude 23-bromo-ketol, of which 15% could be extracted by Girard reagent P; this "ketonic fraction" has been identified as 23*a*-bromo-3β : 11β-dihydroxy-5α : 25*D*-spirostan-12-one (see below). The unreactive portion was essentially the required ketol (VII; R = H), for acetylation followed by debromination converted it into 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one (VIII; R = Ac) in some 50% yield (based on the dibromo-compound). An additional complication in the use of this method of hydrolysing the dibromo-compound was the occurrence of dehydrobromination, the ultraviolet spectra of the crude products indicating the presence of up to 10% of 9(11)-dehydrohecogenin acetate.

In place of methanol other solvents tried were ethanol, propan-2-ol, diethylene glycol (at 110—120°), and acetone (all mixed with water) but they were no more satisfactory: the products all contained appreciable quantities of Girard-reactive material and some of them were badly discoloured. Excellent results, however, attended the use of dioxan or *tert.*-butyl alcohol. With either of these (used in a two-phase system with aqueous sodium hydroxide) the crude products contained little or no αβ-unsaturated ketone or material extractable by Girard reagent P; and acetylation, with subsequent debromination, then gave the required ketol diacetate (VIII; R = Ac) in about 80% yield, based on dibromohecogenin acetate. Furthermore, the yield of this diacetate (VIII; R = Ac) was little lower when the crude mixture of dibromo-compounds, obtained from hecogenin acetate (I) in acetic acid, benzene or dioxan, was used in place of pure 11α : 23*a*-dibromohecogenin acetate.

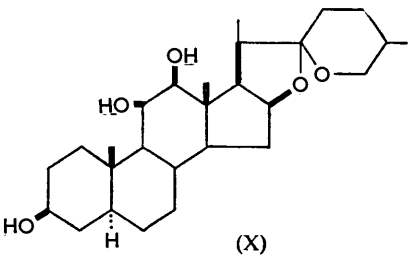
Certain other esters (VIII) were prepared in connection with the experiments described in the next paper; the dibenzoate, dimethanesulphonate, and di*iso*butyrate were obtained by standard methods. However, only the 3-monopivalate could be obtained, presumably because of steric hindrance in ring C. The 3-monoacetate was prepared by treatment of the diol (VIII; R = H) with acetic acid and acetic anhydride (cf. ref. 4) and was converted into the 3-acetate 12-methanesulphonate.

Since the treatment of dibromohecogenin acetate with alkali might lead not only to the desired 12β-hydroxy-11-ketone, but also to other isomeric 11 : 12-ketols, it seemed desirable to have these ketols for reference, and methods for their preparation have been investigated.

The 11β-hydroxy-12-ketone was obtained as its 23*a*-bromo-derivative (IX) by gentle hydrolysis of 11α : 23*a*-dibromohecogenin acetate (VI) or the corresponding free alcohol with ethanolic sodium hydroxide. Girard separation served to remove the unreactive 12β-hydroxy-11-ketone and, after acetylation, the monoacetate (IX; R = H) was obtained



(IX)



(X)

in poor yield. The reactivity of the ketone group to ketonic reagents proved it to be at position 12 rather than 11, and the β-configuration of the 11-hydroxy-group was shown by reduction with lithium aluminium hydride and subsequent debromination by zinc, which converted the ketol into 5α : 25*D*-spirostan-3β : 11β : 12β-triol (X).[16] In addition to the monoacetate (IX; R = H), the 3β : 11β-diacetoxy-12-ketone (IX; R = Ac) was isolated in small yield. Its structure was shown both by its slow formation from the monoacetate (IX; R = H) by acetic anhydride and pyridine at room temperature and by its reduction to the 3β : 11β : 12β-triol (X). The acetylation of the 11β-hydroxy-group under

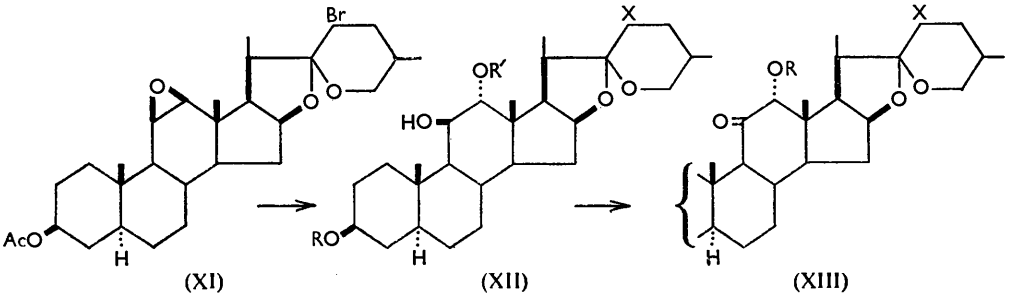
[16] Djerassi, Martinez, and Rosenkranz, *J. Org. Chem.*, 1951, **16**, 1278.

mild conditions may be associated with the presence of the 12-oxo-group; there are reports of the acetylation of isolated 11β-hydroxy-groups by acetic anhydride and pyridine,[17,18] but this reaction is probably slower even than that of our ketol.

Attempts to debrominate the spirostans (IX; R = H and Ac) with zinc in acetic acid were complicated by other changes. The former underwent rearrangement to yield 3β-acetoxy-12β-hydroxy-5α : 25*D*-spirostan-11-one (IV; R = Ac, X = H) (see below), whereas the latter lost its 11β-acetoxy-group as well as the bromine atom and gave hecogenin acetate (I).

Mueller *et al.*[10] prepared the free diol corresponding to (IX) by a method similar to ours and claimed also to have prepared 3β-acetoxy-11β-hydroxy-5α : 25*D*-spirostan-12-one (IX; R = H; H in place of Br) by alkaline hydrolysis of dibromohecogenin acetate, with subsequent perchloric acid-catalysed acetylation (without intermediate purification) and debromination with zinc in acetic acid. In view of our observations on the comparative ease of acetylation of the 11β-hydroxy-group in the monoester (IX; R = H) and also on the reactions of it and the diacetate with zinc and acetic acid, this reputed isolation of the 11β-hydroxy-12-ketone is rather surprising. Rosenfeld and Gallagher [19] recently described an experiment, similar to that of Mueller *et al.*, which yielded hecogenin acetate and, if the conditions of debromination were mild, a compound they believed to be a 3β : 11-diacetoxy-5α : 25*D*-spirostan-12-one. This is in accord with our experiments described above; the diacetoxy-compound can be assigned the 3β : 11β-structure (IX; R = Ac; H in place of Br) by analogy with our 23-bromo-derivative, by the difference of its rotation (+39°) from that of the 11α-epimer (XV) (−42°),[20] and by the similarity of its rotation to that of the diacetate (IX; R = Ac) (+32°) (bromination at $C_{(23)}$ has a small, irregular effect on rotation).

For the preparation of 3β : 12α-diacetoxy-5α : 25*D*-spirostan-11-one (XIII; R = Ac, X = H) and its 23*a*-bromo-derivative (XIII; R = Ac, X = Br), 3β-acetoxy-23*a*-bromo-11β : 12β-epoxy-5α : 25*D*-spirostan (XI) [2,3] was first treated with trichloroacetic acid.[21] The non-crystalline product is believed to have been essentially the 11β-hydroxy-12α-trichloroacetoxy-compound (XII; R = Ac, R′ = CCl_3·CO, X = Br) in view of the analogous

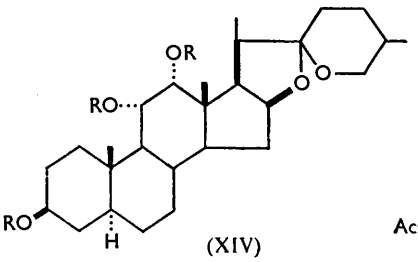


opening of 11β : 12β-epoxides with hydrogen halides to the 11β-hydroxy-12α-halogeno-compounds.[2,3,21] Alkaline hydrolysis of the trichloroacetate gave 23*a*-bromo-5α : 25*D*-spirostan-3β : 11β : 12α-triol (XII; R = R′ = H, X = Br), which was debrominated by zinc and acetic acid to the halogen-free triol (XII; R = R′ = X = H). The triols gave only diacetates under normal acetylating conditions, and these are assigned the structures (XII; R = R′ = Ac, X = Br and H, respectively). Finally, oxidation of the triol diacetates with the chromic anhydride–pyridine complex gave the required 12α-acetoxy-11-ketones (XIII; R = Ac, X = Br and H, respectively). The former was converted into the latter by treatment with zinc in acetic acid. Baumgartner and Tamm [22] recently

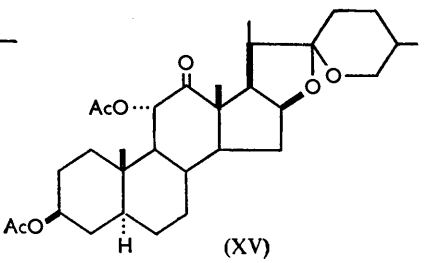
[17] Steiger and Reichstein, *Helv. Chim. Acta*, 1937, **20**, 817.
[18] Kemp, Kappas, Salamon, Herling, and Gallagher, *J. Biol. Chem.*, 1954, **210**, 123.
[19] Rosenfeld and Gallagher, *J. Amer. Chem. Soc.*, 1955, **77**, 4367.
[20] Wendler, Hirschmann, Slates, and Walker, *ibid.*, p. 1632.
[21] Cf. Fürst and Scotoni, *Helv. Chim. Acta*, 1953, **36**, 1410.
[22] Baumgartner and Tamm, *ibid.*, 1955, **38**, 441.

described the preparation of methyl 3α : 12α-diacetoxy-11-oxocholanoate by a method analogous to that described above for the preparation of (XIII). By using acetic acid rather than trichloroacetic acid, they obtained the intermediate triol diacetate directly, but their yield was poor.

The structures assigned to the 12α-hydroxy-compounds were confirmed as follows : the 5α : 25*D*-spirostan-3β : 11 : 12-triol, prepared by the action of osmium tetroxide on the Δ^{11}-olefin,[23] readily formed a triacetate and must, therefore, be the 3β : 11α : 12α-triol (XIV; R = H). The structures of the 3β : 11α : 12β-triol and the 3β : 11β : 12β-triol have been convincingly demonstrated by Wendler *et al.*[20] As our triol, prepared from the 3β-hydroxy-11β : 12β-epoxide, differs from these three, it must, by exclusion, be the 3β : 11β : 12α-triol. The paper-chromatographic behaviour of the isomeric triols is to be discussed in a later Part of this series.[24]



(XIV)



(XV)

The structure of our 12α-hydroxy-11-ketone (XIII; R = X = H) appears to be soundly based on the method of preparation, but additional evidence is derived from (*a*) the reduction of the diacetate (XIII; R = Ac, X = H) to 11-oxotigogenin, indicating the presence of an 11-oxo-group (see next paper), and (*b*) its non-identity with the 12β-hydroxy-11-ketone (VIII), the structure of which has been proved by Wendler *et al.*[20]

An attempt to obtain the remaining ketol, *i.e.*, the 11α-hydroxy-12-ketone, as its diacetate (XV)[20] by epimerisation of the 11β-acetoxy-12-ketone (IX; R = Ac) and debromination was unsuccessful, the latter compound being recovered unchanged after treatment with acetic acid, alone or in presence of perchloric or toluene-*p*-sulphonic acid.

Properties of the Isomeric 11 : 12-*Ketols.—Infrared spectra* (with Dr. J. E. Page). When the hydroxyl group in ring C is not esterified, the ketols described above display the expected infrared absorption (see Table, Nos. 7, 9, and 11, also Experimental section). For the ketol diacetates, on the other hand, there is no maximum at the normal C=O stretching frequency for a ketone; instead, there is, in the 1700 cm.$^{-1}$ region, (*a*) a strong band at about 1730 cm.$^{-1}$, which we attribute to the combined effects of the 3β-acetoxy-group and the ketone group of ring C, the absorption of the latter having been displaced by the neighbouring acetoxy-group, and (*b*) a band at about 1750 cm.$^{-1}$ (1740 cm.$^{-1}$ for No. 6), which can be attributed to the acetoxy-group of ring C, the absorption having been displaced from the normal C=O stretching frequency by the neighbouring keto-group. Bands at about 1240 and 1220 cm.$^{-1}$ are, again, attributed to normal and displaced acetate absorption (C–O stretching)[13,25] (Table, Nos. 6, 8, 10, 12).

These results, which are in general agreement with those quoted by Jones and Herling[26] for 11 : 12-ketol derivatives, invite comparison with the spectra of steroid α-bromo-ketones. The absorption due to a ketone group is displaced to higher frequencies by an equatorial, but not by an axial, bromine atom attached to the neighbouring carbon atom;[13,14] it appears, however, that an acetoxy-group can cause a similar displacement irrespective of its configuration. Nevertheless, the literature does not suggest that this is a regular phenomenon : there appears to be but little mutual interaction between a 20-oxo- and a

[23] Hirschmann, Snoddy, Hiskey, and Wendler, *J. Amer. Chem. Soc.*, 1954, **76**, 4013.
[24] Brooks, Hunt, Long, and Mooney, *J.*, in the press.
[25] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2820.
[26] Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252.

17-acetoxy-group in either of the possible configurations,[25,26,27] whereas in the 17*a*-acetoxy-17-oxo-D-homosteroids the equatorial 17*a*β-epimer shows a considerable displacement of both ketone and acetoxy-absorption (max. at 1729 and 1756 cm.$^{-1}$ respectively) in contrast to the axial 17*a*α-epimer (max. at 1716 and 1737 cm.$^{-1}$ respectively).[26]

Jones *et al.*[14,25] suggest that a field effect is responsible for the displacements observed in both the bromo- and the acetoxy-ketones and that with the former it operates only when

Physical properties of some of the 11 : 12-*ketols and their derivatives.**

No.	Compound	Infrared absorption † $\nu_{max.}$ (1700 region) (cm.$^{-1}$)	$\nu_{max.}$ (1200 region) (cm.$^{-1}$)	Ultraviolet absorption in EtOH $\lambda_{max.}$ (mμ)	log ε	$[M]_D$
1	11-Oxotigogenin	1706	—	295—303	1·40	−133°
2	11-Oxotigogenin acetate (II)	1708, 1730	1240	298—304	1·38	−184
3	Hecogenin	1710	—	284—290	1·65	+30
4	Hecogenin acetate (I)	1706, 1732	1238	287	1·58	−12
5	23*a*-Bromohecogenin acetate	1712, 1736	1240	288	1·63	−77
6	3β : 11α-Diacetoxy-5α : 25*D*-spirostan-12-one (XV)	1729, 1740	—	—	—	−224
7	3β-Acetoxy-23*a*-bromo-11β-hydroxy-5α : 25*D*-spirostan-12-one (IX; R = H)	1705, 1732	1240	307	1·65	+17
8	3β : 11β-Diacetoxy-23*a*-bromo-5α : 25*D*-spirostan-12-one (IX; R = Ac)	1720, 1735, 1750	1218, 1238	303—306	1·90	+195
9	3β : 12α-Dihydroxy-5α : 25*D*-spirostan-11-one (XIII; R = X = H)	1703	—	306—320	1·75	−59
10	3β : 12α-Diacetoxy-5α : 25*D*-spirostan-11-one (XIII; R = Ac, X = H)	1735, 1756	1220, 1238	310	1·84	+28
11	3β : 12β-Dihydroxy-5α : 25*D*-spirostan-11-one (VIII; R = H)	1708	—	290	1·56	−185
12	3β : 12β-Diacetoxy-5α : 25*D*-spirostan-11-one (VIII; R = Ac)	1730, 1750	1230, 1236	293	1·47	−421

Group	Conformation	Differences $\Delta\lambda_{max.}$ (mμ) ‡	ΔM ‡
12β-Hydroxy	e	−9 (−12)	−50° (+77°)
11α-Acetoxy	e	—	−212 (−282)
12β-Acetoxy	e	−8 (−5)	−237 (−24)
11β-Hydroxy	a	+19 (+15 to +23)	+94 (+63)
12α-Hydroxy	a	+14	+74 (+36)
11β-Acetoxy	a	+16 (+7 to +11)	+272 (+158)
12α-Acetoxy	a	+9	+212 (+322)

* All determinations made in these laboratories except for No. 6, in which instance the figures are taken from ref. 20.

† All measurements made in CS_2, except for item 9, where chloroform was the solvent.

‡ Figures in parentheses are corresponding values for the cholanic acid series. For references see text.

the C–Br bond is roughly coplanar with the C=O bond (as in the equatorial bromo-compounds). In the acetoxy-ketones, the relative dispositions of the two C=O bonds are not fixed in this way, and this may account for the decidedly less regular effects upon the infrared absorption.

Ester groupings other than acetate can also cause a displacement of the C=O stretching frequency of a neighbouring ketone group. Thus, in the esters of 3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one, a 12β-methanesulphonyloxy- or 12β-*iso*butyryloxy-group causes the ketone band to appear at about 1730 cm.$^{-1}$; a benzoyloxy-group has a smaller effect, the ketone band occurring at 1718 cm.$^{-1}$. Although in the last two instances the reciprocal effect can be observed in the displacement of the C=O stretching frequency of the ester groupings (to 1746 and 1730 cm.$^{-1}$ respectively), it is less clear whether the same is true of the C–O stretching frequency in these esters.

The spectra of the di*iso*butyrate (VIII; R = Pr^{i}·CO), the 3-monopivalate (IV; R = Bu^{t}·CO, X = H), and the dibenzoate (VIII; R = Bz) showed C–O stretching bands at positions agreeing with those found by Thompson and Torkington in simple alkyl esters [28] and with those found by us in the corresponding *cyclo*hexyl esters.

[27] Turner, *J. Amer. Chem. Soc.*, 1953, **75**, 3489.
[28] Thompson and Torkington, *J.*, 1945, 640.

Again, the 3-acetate 12-methanesulphonate and the 3 : 12-dimethanesulphonate of the ketol (VIII; R = H) absorbed within the ranges suggested by Colthup [29] for a covalent sulphonate group.

Ultraviolet spectra. Studies of the 11 : 12-ketols in the cholanic acid series have shown that the position of the weak ketone band is displaced by a neighbouring hydroxy- or acetoxy-group, the direction of the shift depending on the conformation of the substituent.[22,30,31] In this respect, such groups resemble similarly placed bromine atoms.[30,32]

It will be seen from the Table that for the sapogenin 11 : 12-ketols and their acetates there are displacements of the ketone band very similar to those observed for the cholanic acid analogues.

Rotations. The Table shows the molecular-rotation contributions of 11- and 12-hydroxy- and -acetoxy-groups in the 11 : 12-ketols. Though the individual values differ considerably from those derived by Baumgartner and Tamm [22] from the 11 : 12-ketols in the cholanic series (and variations in their solvents may account for part of the difference [33]), a similar pattern can be discerned. In particular, in both series an axial acetoxy-group makes a strongly positive contribution to the molecular rotation, whereas an equatorial acetoxy-group has the opposite effect (though, in the cholanic series, the ΔM value for a 12β-acetoxy-group is only −24°). Again, in both series, acetylation of an axial hydroxy-group changes the ΔM value in a positive sense, whereas acetylation of an equatorial hydroxy-group results in a negative change of molecular rotation.

Paper chromatography. This will be discussed in a later Part of this series.[24]

Interconversion of the ketols. The formation of a 12β-hydroxy-11-ketone from an 11-bromo-12-ketone under the action of alkali involves initial hydrolysis, with inversion, to an 11-hydroxy-12-ketone, and subsequent rearrangement, presumably through an 11-ene-11 : 12-diol or an ionised form thereof.[10,19,34] Ketonisation of the enediol might give rise to any of the four isomeric ketols, and the proportions in which they occur in the equilibrium mixture will depend on their relative stabilities under the conditions employed.

The preparation of the diacetate (VIII; R = Ac) from dibromohecogenin acetate in 80% yield suggests that the equilibrium mixture in this series consists almost entirely of the 12β-hydroxy-11-ketone. This is borne out by the published statement that the bromo-ketol (VII; R = H) is unaffected by vigorous treatment with caustic alkali,[10] as well as by our own experiments on the stability of the debrominated ketol (VIII; R = H) to alkali.

Both the 11β-hydroxy-12-ketone (IX; R = H) and the 11β-acetoxy-12-ketone (IX; R = Ac) were readily rearranged to 23*a*-bromo-3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one (VII; R = H) by a boiling solution of sodium hydroxide in aqueous *tert.*-butyl alcohol. The monoacetate was also rearranged slowly by caustic alkali at room temperature and quickly by boiling methanolic hydrochloric acid. More surprising was the observation that the 11β-hydroxy-12-ketone (IX; R = H) was converted into 3β-acetoxy-23*a*-bromo-12β-hydroxy-5α : 25*D*-spirostan-11-one (IV; R = Ac, X = Br) by acetic acid at 100°; this unexpectedly easy rearrangement explained the conversion of the former compound (IX; R = H) into the 12-hydroxy-11-ketone (IV; R = Ac, X = H) under the action of zinc and acetic acid (see above).

The 12α-hydroxy-11-ketones (XIII) were far more stable to both acid and alkaline conditions than were the 11β-hydroxy-12-ketones. The diacetate (XIII; R = Ac, X = H), for example, was merely hydrolysed to the corresponding diol by a boiling solution of sodium hydroxide in aqueous *tert.*-butyl alcohol (this is discussed further below). On more vigorous treatment with alkali, the ketol was epimerised to the 12β-hydroxy-11-ketone (VIII; R = H), but it was unaffected by prolonged boiling with 2N-alcoholic hydrochloric acid.

[29] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397.
[30] Cookson and Dandegaonker, *J.*, 1955, 352.
[31] Schindler and Reichstein, *Helv. Chim. Acta*, 1954, **37**, 667.
[32] Cookson, *J.*, 1954, 282.
[33] Cf. Norymberski, *J.*, 1954, 762.
[34] Gallagher and Long, *J. Biol. Chem.*, 1946, **162**, 521; Gallagher and Hollander, *ibid.*, p. 533; Gallagher, *ibid.*, p. 539.

Finally, it should be mentioned that Wendler *et al.*[20] have reported that the 11α-acetoxy-12-ketone (XV) is converted quantitatively into the 12β-hydroxy-11-ketone (VIII; R = H) by boiling 2N-methanolic potassium hydroxide.

The ease of rearrangement of the 11β-hydroxy-12-ketone compared with that of the 12α-hydroxy-11-ketone stands in contrast with the enol acetylation of 11-oxo-steroids under conditions that have no effect upon 12-oxo-compounds.[35,36] However, enol acetylation of an 11-ketone, unsubstituted at position 12, gives the 11-acetoxy-$\Delta^{9(11)}$-compound;[7b,36,37] if this is also the preferred direction of enolisation in the ketol (XIII), the sluggishness of the epimerisation may be explained.

Reference has been made above to the stability of the 12α-hydroxy-11-ketone (XIII; R = X = H) under the alkaline conditions that convert dibromohecogenin acetate into the 12β-hydroxy-11-ketone. This implies that the bromo-compound (XIII; R = H, X = Br) is not an intermediate in this reaction and, hence, that the kinetically as well as the thermodynamically controlled protonation of the common enediol at $C_{(12)}$ occurs entirely, or nearly so, in the axial α-position. Corey[38] has recently advanced the theory that in the kinetically controlled ketonisation of an enolised *cyclo*hexanone, the incoming substituent adopts the axial configuration preferentially; the theory was supported by much experimental evidence drawn from bromination of ketones, but none was offered to support the belief that the rule applies also to protonation of enols. Our findings now provide one piece of experimental evidence to support this aspect of Corey's theory.

The formation in this series of the 12β-hydroxy-11-ketone as virtually the sole product of the action of alkali on the isomeric ketols is different from the situation in the cholanic acid series, in which the 12β-hydroxy-11-ketone, 11α-hydroxy-12-ketone, 12α-hydroxy-11-ketone, and 11β-hydroxy-12-ketone were isolated in yields of 63·1, 30·4, 1·1%, and "a trace," respectively.[8] The difference cannot be a result of the different configurations at $C_{(5)}$, or of the presence of an acidic side chain in only one of the series of compounds, since Gallagher[39] has shown that 3α : 12β-dihydroxy-11-oxoetianic acid is stable to alkali. The factors influencing the relative stabilities of the 12-hydroxy-11-ketones and 11-hydroxy-12-ketones remain obscure, although the nature of the side chain is clearly important. There is, indeed, other evidence that reactions at $C_{(11)}$ and $C_{(12)}$ in the spirostan and the etianic acid series are similar, and that they differ from those in the cholanic acid series, and this has been attributed to the steric effect of the long, freely rotating cholanic acid side chain.[10]

Experimental

For general experimental information, see Part XIII.

11α : 23a-*Dibromohecogenin Acetate* (VI).—A suspension of hecogenin acetate (100 g.) in dry benzene (150 ml.) was treated with a few ml. of a 4·0N-solution of bromine in benzene. When the colour had been discharged, the remainder of the bromine solution (245 ml. in all) was added during 10 min. with continual swirling. During this time, the hecogenin acetate dissolved, an orange solid (probably a complex of hecogenin acetate with bromine) separated, and this, in turn, went into solution. The solvent was then removed rapidly under reduced pressure at room temperature and the residual gum was dissolved in boiling ethanol (1 l.) (swirling is necessary to effect rapid dissolution); 11α : 23*a*-dibromohecogenin acetate separated almost immediately and after the mixture had cooled to room temperature the solid was filtered off, washed with a little cold ethanol, and dried. The product (70·6 g., 53%) had m. p. 180—182° (decomp.) and $[\alpha]_D$ −38°. For infrared spectrum see ref. 13. Reported m. p.s of this compound vary between 180—183° (decomp.) and 189—191° (decomp.); the rotation is given as −38° and −39·3°.[2,5,15]

The mother-liquors from the crystallisation were added, without undue delay, to a zinc–copper couple, which had been freshly prepared from zinc dust (200 g.) and copper sulphate solution (15% w/v; 1350 ml.) and washed with ethanol. The mixture was boiled under reflux with stirring for 3 hr., and filtered while hot. The solid residue was washed with methylene

[35] Hirschmann, Brown, and Wendler, *J. Amer. Chem. Soc.*, 1951, **73**, 5373.
[36] Hirschmann and Wendler, *ibid.*, 1953, **75**, 2361.
[37] Crawshaw, Henbest, and Jones, *J.*, 1954, 731.
[38] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.
[39] Gallagher, *J. Biol. Chem.*, 1946, **165**, 211.

chloride, and the combined filtrate and washings were concentrated under reduced pressure to *ca.* 500 ml. Water and 2N-hydrochloric acid (50 ml.) were added and the crude hecogenin acetate was filtered off, washed with water, and dried. Crystallisation from chloroform–methanol gave material (32 g.) suitable for rebromination.

11α : 23a-*Dibromohecogenin*.—A solution of the acetate (5·0 g.) in benzene (75 ml.) and methanol (500 ml.) was treated with concentrated hydrochloric acid (5 ml.) and the solution was left at room temperature for 24 hr. The solvents were removed under reduced pressure and the residue was dissolved in a little methanol. 11α : 23a-*Dibromohecogenin* (3·63 g.) gradually separated as needles that decomposed between 181° and 189° and had $[\alpha]_D$ −34°; a second crop weighed 0·40 g. (total yield 86%) and had similar constants. Further crystallisation from methanol gave material, decomp. *ca.* 180°, $[\alpha]_D$ −33° (Found: C, 55·1; H, 6·7. $C_{27}H_{40}O_4Br_2$ requires C, 55·1; H, 6·85%). Infrared spectrum: see ref. 13.

Bromination of Hecogenin Acetate in Carbon Tetrachloride.—A solution of hecogenin acetate (30 g.) in carbon tetrachloride (600 ml.) was stirred while bromine (6·75 ml.) in carbon tetrachloride (50 ml.) was added during 15 min. After a further 15 min., the solvent was removed under reduced pressure and 11α : 23*a*-dibromohecogenin acetate (19·5 g., 49%) isolated as described in the previous experiment.

The ethanol mother-liquors were evaporated to dryness under reduced pressure and the residual gum was chromatographed in 3 : 2 benzene–light petroleum on acid-washed alumina (400 g.; Peter Spence, Grade H). Benzene–light petroleum (1 : 1) eluted crude 11α : 23b-*dibromohecogenin acetate* (6·4 g.) which, crystallised first from methanol, then from 3 : 1 methanol–ethyl acetate, gave needles (4 g., 10%), m. p. 168—169° (decomp.) (depressed on admixture with 11α : 23*a*-dibromohecogenin acetate), $[\alpha]_D$ −46° (Found: C, 55·2; H, 6·9; Br, 24·8. $C_{29}H_{42}O_5Br_2$ requires C, 55·3; H, 6·7; Br, 25·35%). Infrared spectrum: see ref. 13. Treatment of the dibromo-compound (0·5 g.) with zinc dust (2·5 g.) in boiling acetic acid (20 ml.) for 2 hr. gave hecogenin acetate (310 mg., 83%), m. p. 243—251°. Its identity was confirmed by infrared spectroscopy.

3β-*Acetoxy*-23b-*bromo*-5α : 25D-*spirost*-9(11)-*en*-12-*one*.—11α : 23*b*-Dibromohecogenin acetate (0·5 g.) in collidine (7 ml.) was boiled under reflux for 1 hr. After being cooled, the solution was diluted with ether, and the precipitated collidine hydrobromide was filtered off. The filtrate was washed with 2N-hydrochloric acid and water, dried, and evaporated. Crystallisation of the residue from ethanol gave the unsaturated ketone as prisms (0·29 g., 67%), m. p. 219—220° (decomp.), $[\alpha]_D$ −47° (in $CHCl_3$), −48° (in dioxan) (Found: Br, 14·2. Calc. for $C_{29}H_{41}O_5Br$: Br, 14·5%), $\lambda_{max.}$ 237·5 mμ (ε 12,700). Infrared spectrum: see ref. 13. Mueller and Norton [15] give m. p. 220—221° (decomp.), $[\alpha]_D$ −47·2° (in dioxan), $\lambda_{max.}$ 238 mμ (ε 13,800).

3β : 12β-*Diacetoxy*-5α : 25D-*spirostan*-11-*one* (VIII; R = Ac).—(a) *From* 11α : 23a-*dibromohecogenin acetate*. The dibromo-compound (50 g.) was boiled under reflux for 6 hr. with a stirred solution of sodium hydroxide (25 g.) in *tert.*-butyl alcohol (500 ml.) and water (500 ml.); the mixture was a two-phase one throughout. Removal of the alcohol by distillation under reduced pressure, dilution of the residue with water to 2 l., and filtration gave the crude crystalline 23-bromo-ketol (VII; R = H) (42·0 g.); treatment with Girard reagent P extracted about 2% of this material. The crude bromo-ketol was boiled under reflux for 1 hr. with pyridine (375 ml.) and acetic anhydride (375 ml.). The solution was evaporated to dryness *in vacuo* and the residue was evaporated with methanol. Debromination of the residue by stirring it with zinc dust (170 g.) in boiling acetic acid (450 ml.) for 2 hr., filtration, and dilution with water gave a crude product (40·5 g.) which, on crystallisation from ethanol, yielded in two crops, 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one (34·1 g., 81%), m. p. 222—225°, $[\alpha]_D$ −78°.

(b) *From hecogenin acetate* via *the crude dibromo-derivative*. A solution of hecogenin acetate (25·0 g.) in dry benzene (200 ml.) was stirred during the addition of bromine (6·2 ml.) in benzene (50 ml.); after the first few ml. had been decolorized, the remainder was added in 5 min. The solution was left for a further 10 min. and was then concentrated *in vacuo* at <20° to about 40 ml. Sodium hydroxide solution (5%; 250 ml.) and *tert.*-butyl alcohol (300 ml.) were added and distillation was continued, with stirring, to remove the residual benzene. Hydrolysis, acetylation, and debromination as in (*a*) gave a first crop (19·8 g., 71%) of the required ketol diacetate, m. p. 224—227°, $[\alpha]_D$ −79°, and, by fractional crystallisation of the residue from ethanol, a further 1·63 g. (6%) of material with similar constants.

A similar yield of 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one was obtained when hecogenin acetate was brominated by the method of Djerassi *et al.*[11] and the crude dibromo-compound treated as above. Again, dioxan could be used for both the bromination and the hydrolysis stage as follows: Hecogenin acetate (25 g.) in dioxan (250 ml.) was treated with bromine

(6·0 ml.) and after being stirred at room temperature for 40 min., the solution was treated with sodium hydroxide (25·0 g.) in water (250 ml.) and boiled under reflux for 6 hr. The crude bromo-ketol so obtained was acetylated and debrominated as described above, to give a first crop of 19·6 g. (70%) of the ketol diacetate.

A sample of 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one, crystallised to constant m. p. from ethanol and from benzene–light petroleum, had m. p. 223—226°, $[\alpha]_D$ −79·5° (*c* 2), $[\alpha]_D$ −72° (*c* 3 in dioxan), $\nu_{max.}$ (in CS_2) 1750 and 1230 (displaced OAc), 1730 (displaced CO), 1730 and 1236 (OAc), 978, 916, and 896 cm.$^{-1}$ (25*D*-spirostan). Djerassi *et al.*[11] give m. p. 225—225·5°, $[\alpha]_D$ −67° ($CHCl_3$); Mueller *et al.*[10] give $[\alpha]_D$ −71·8° (dioxan).

3β : 12β-*Diacetoxy*-23a-*bromo*-5α : 25D-*spirostan*-11-*one* (VII; R = Ac).—11α : 23*a*-Dibromohecogenin acetate (50 g.) was treated with alkali as described in experiment (*a*) above and the crude bromo-ketol (38·4 g.) obtained after treatment with Girard reagent was acetylated for 2 hr. with acetic anhydride (60 ml.) and pyridine (60 ml.) at the b. p. The acetylating mixture was removed under reduced pressure and the residue dissolved in acetic acid (300 ml.). Dilution with water (3 l.) gave a solid that melted at 196° after crystallisation from methanol (yield 28·8 g., 60%). After further crystallisation from the same solvent, the *ketol diacetate* had m. p. 196—198°, $[\alpha]_D$ −66° (Found: C, 61·4; H, 7·4; Br, 13·0. $C_{31}H_{45}O_7Br$ requires C, 61·1; H, 7·4; Br, 13·1%). Infrared spectrum: see ref. 13.

Debromination of this compound with zinc in boiling acetic acid gave a 92% yield of 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one (VIII; R = Ac).

Hydrolysis of the bromo-ketol diacetate with a boiling 3% solution of potassium hydroxide in 85% aqueous methanol for 1 hr. gave 23*a*-bromo-3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one (VII; R = H), crystallising from aqueous methanol in needles, which melted at 135°, resolidified, and melted finally at 208—210°, $[\alpha]_D$ −33° (in $CHCl_3$), −29° (*c* 1 in dioxan). For analysis it was dried at 120°/0·05 mm. (Found: C, 61·4; H, 7·8; Br, 14·9. Calc. for $C_{27}H_{41}O_5Br$: C, 61·7; H, 7·9; Br, 15·2%). Infrared spectrum: ref. 13. Mueller *et al.*[10] give m. p. 233—234° (decomp.), $[\alpha]_D$ −23·7° (dioxan).

3β-*Acetoxy*-23a-*bromo*-12β-*hydroxy*-5α : 25D-*spirostan*-11-*one* (IV; R = Ac, X = Br).—A mixture of 23*a*-bromo-3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one (5·0 g.), acetic acid (50 ml.), and acetic anhydride (5·0 ml.) was boiled for 1 hr.; water (25 ml.) was added and the mixture refluxed for a further 30 min. Water (*ca.* 200 ml.) was gradually added to the hot mixture and, after cooling, the solid was filtered off. Crystallisation from aqueous ethanol (charcoal) gave the *monoacetate* (3·7 g., 69%) as needles, m. p. 214° (decomp.), $[\alpha]_D$ −41·0° (*c* 1·3) (Found: C, 61·7; H, 7·6; Br, 13·9. $C_{29}H_{43}O_6Br$ requires C, 61·4; H, 7·65; Br, 14·1%), $\nu_{max.}$ (in CS_2) 3500 (OH), 1734 and 1240 (OAc), 1710 (CO), 1010, 945, 918, and 726 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

3β : 12β-*Dihydroxy*-5α : 25D-*spirostan*-11-*one and Various Esters thereof.*—*Diol* (VIII; R = H). This was prepared by hydrolysis of the diacetate with a boiling 3% solution of sodium hydroxide in 90% aqueous methanol for 3 hr. It separated from aqueous methanol or aqueous acetone as a hydrate, m. p. 212—214°, $[\alpha]_D$ −40° (*c* 1 in $CHCl_3$), −39° (*c* 1·5 in dioxan). The hydrate lost its water at 120° in a high vacuum. The diol had infrared max. (in CS_2) at 3620 and 3500 (OH), 1708 (CO), 976, 916, and 896 cm.$^{-1}$ (25*D*-spirostan). Mueller *et al.*[10] give m. p. 217—218°, $[\alpha]_D$ −40° (dioxan). The rotation (−13° in $CHCl_3$) given by Djerassi *et al.*[11] is presumably incorrect.

3-*Monoacetate* (IV; R = Ac, X = H). The ketol hydrate (20·0 g.) was boiled for 1 hr. with acetic acid (200 ml.) and acetic anhydride (20 ml.). Water (200 ml.) was gradually added to the boiling solution and, after cooling, the mixture was further diluted with water to *ca.* 1 l. and filtered. Crystallisation of the solid from methanol gave the 3-monoacetate (11·6 g., 55%) as prisms, m. p. 214—218°, $[\alpha]_D$ −48° (*c* 1) (Found: C, 71·5; H, 9·2. Calc. for $C_{29}H_{44}O_6$: C, 71·3; H, 9·1%), $\nu_{max.}$ (in CS_2) 3500 (OH), 1733 and 1236 (OAc), 1708 (CO), 976, 916, and 896 cm.$^{-1}$ (25*D*-spirostan). Djerassi *et al.*[4] give m. p. 212—215°, $[\alpha]_D$ −30°.

3-*Acetate* 12-*methanesulphonate*. The 3-monoacetate (12 g.) in pyridine (70 ml.) was cooled in ice while methanesulphonyl chloride (7 ml.) was added dropwise. After being kept overnight at room temperature, the solution was poured on ice, and the precipitate extracted with benzene. The extract was washed with 2N-hydrochloric acid and water, then evaporated to dryness, and the residue crystallised from methanol. 3β-*Acetoxy*-12β-*methanesulphonyloxy*-5α : 25D-*spirostan*-11-*one* (12·6 g., 90%) had m. p. 173—175°, raised by further crystallisation to 174—176°, $[\alpha]_D$ −64° (*c* 1) (Found: C, 63·8; H, 8·3. $C_{30}H_{46}O_8S$ requires C, 63·6; H, 8·2%), $\nu_{max.}$ (in CS_2) 1730 and 1240 (OAc), 1730 (displaced CO), 1360 and 1175 (methanesulphonate), 976, 917, and 895 cm.$^{-1}$ (25*D*-spirostan). The same compound could be prepared in 90% overall

yield from the free ketol by monoacetylation as above, followed by methanesulphonylation of the uncrystallised monoacetate.

3-*Monopivalate* (IV; R = Bu^t·CO, X = H). Treatment of the ketol (4·0 g.) in pyridine (20 ml.) with pivalyl chloride (4 ml.) overnight at room temperature, isolation with ether, and crystallisation from ethanol gave the 3-*monopivalate* (3·6 g., 77%), m. p. 229—237°. After crystallisation from acetone, it had m. p. 232—236°, $[\alpha]_D$ −41° (Found: C, 72·6; H, 9·6. $C_{32}H_{50}O_6$ requires C, 72·4; H, 9·5%), $\nu_{max.}$ (in CS_2) 3500 (OH), 1723, 1280, 1162, and 1145 (trimethylacetate), 1708 (CO), 980, 920, and 899 cm.$^{-1}$ (25*D*-spirostan).

3 : 12-*Dibenzoate* (VIII; R = Bz). Treatment of the ketol (3·0 g.) with benzoyl chloride (3·0 ml.) in pyridine (40 ml.) overnight at room temperature gave the *dibenzoate*, crystallising from methanol in plates (2·6 g., 61%), m. p. 280—285°, $[\alpha]_D$ −61° (*c* 1) (Found: C, 75·1; H, 7·8. $C_{41}H_{50}O_7$ requires C, 75·2; H, 7·7%), $\nu_{max.}$ (in CS_2) 1730 (displaced benzoate), 1718, 1265, 1112, and 716 (benzoate), 1718 (displaced CO), 980, 918, 898, and 862 cm.$^{-1}$ (25*D*-spirostan).

3 : 12-*Diisobutyrate* (VIII; R = Pr^i·CO). Treatment of the ketol (5·0 g.) with *iso*butyryl chloride (10 ml.) in pyridine (20 ml.) at room temperature for 65 hr., followed by precipitation and crystallisation from ethanol, gave the *diisobutyrate* (3·67 g., 58%), m. p. 192—197°. After further crystallisation it had m. p. 198—202°, $[\alpha]_D$ −65° (*c* 1) (Found: C, 72·1; H, 9·0. $C_{35}H_{54}O_7$ requires C, 71·6; H, 9·3%), $\nu_{max.}$ (in CS_2) 1746 (displaced *iso*butyrate), 1728, 1240, 1188, and 1152 (*iso*butyrate), 1728 (displaced CO), 978, 916, and 896 cm.$^{-1}$ (25*D*-spirostan).

3 : 12-*Dimethanesulphonate* (VIII; R = Me·SO_2). The ketol (1 g.) was treated with methanesulphonyl chloride (2 ml.) in pyridine (10 ml.) overnight at room temperature. Isolation with benzene and crystallisation from benzene–methanol gave the *dimethanesulphonate* (1·12 g., 86%), m. p. 165—166° (decomp.) (Found: S, 10·3. $C_{29}H_{46}O_9S_2$ requires S, 10·6%), $\nu_{max.}$ (in Nujol) 1726 (displaced CO), 1360 and 1175 (methanesulphonate), 978, 918, and 895 cm.$^{-1}$ (25*D*-spirostan).

3β-*Acetoxy*-23a-*bromo*-11β-*hydroxy*-5α : 25D-*spirostan*-12-*one* (IX; R = H).—11α : 23*a*-Dibromohecogenin (2 g.) was dissolved in hot ethanol (320 ml.), the solution was cooled to room temperature, and 40% sodium hydroxide solution (17 ml.) was added. After 30 min., the solution was acidified with a slight excess of acetic acid and evaporated to small bulk under reduced pressure. Dilution of the residue with water gave a solid (1·82 g.), $[\alpha]_D$ −13°. This material (1·78 g.) was boiled under reflux for 1 hr. in ethanol (30 ml.) containing Girard reagent P (1 g.) and acetic acid (3 ml.). The solution was poured into water (200 ml.) containing sodium hydrogen carbonate (5 g.), a trace of solid was filtered off, and the solution was acidified with hydrochloric acid. The precipitated solid (1·68 g.) was acetylated overnight at room temperature with pyridine (10 ml.) and acetic anhydride (10 ml.). The solid obtained by precipitation with water was triturated with methanol and then yielded a microcrystalline solid which, on crystallisation from ethanol, gave the 3-*monoacetate* (0·48 g., 27%), m. p. 201—209° (decomp.), $[\alpha]_D$ +2·7° (*c* 0·5) (Found: C, 61·0; H, 7·6; Br, 14·0. $C_{29}H_{43}O_6Br$ requires C, 61·35; H, 7·6; Br, 14·1%), $\nu_{max.}$ (in Nujol) 3460 (OH), 1710 and 1266 (OAc), 1012, 946, 918, 864, and 726 cm.$^{-1}$ (23a-bromo-25*D*-spirostan). On one occasion, the compound was obtained as prisms, m. p. 218°, $[\alpha]_D$ +3°; crystallisation from acetone or ethanol then gave needles. The infrared spectra of the two crystal forms were distinct in Nujol, that of the prisms being as follows: 1735 and 1240 (OAc), 1705 (CO), 1012, 946, 918, 862, and 726 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan). In bromoform solution, both forms showed identical spectra (see also ref. 40).

The compound gave a precipitate on brief warming in ethanol with Johnson's 2 : 4-dinitrophenylhydrazine–phosphoric acid reagent.[41]

Treatment of the ketol with toluene-*p*-sulphonhydrazide in acetic acid at room temperature gave the *toluene*-p-*sulphonylhydrazone*, m. p. 227—229° (decomp.), $[\alpha]_D$ −32° (*c* 0·99) after crystallisation from chloroform–methanol (Found: C, 58·9; H, 7·4; S, 4·35. $C_{36}H_{51}O_7N_2BrS$ requires C, 58·8; H, 7·0; S, 4·4%), $\nu_{max.}$ in (Nujol) 3620 (OH), 3200 (NH), 1731 and 1255 (OAc), 1350 and 1160 (SO_2·NH), 1007, 952, 920, and 724 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

3β : 11β-*Diacetoxy*-23a-*bromo*-5α : 25D-*spirostan*-12-*one* (IX; R = Ac).—(a) *From* 11α : 23a-*dibromohecogenin acetate*. The dibromo-compound (50 g.) was boiled for 2 hr. with potassium hydroxide (12·5 g.) in 95% methanol (500 ml.). The solution was diluted with water, and the precipitated solid was filtered off. Treatment of this solid with Girard reagent P, as described in the last experiment, yielded 20·9 g. of reactive ketone, which crystallised from methanol as needles (15·0 g.), m. p. 192—195° (decomp.). This crude solid was acetylated for 30 min. on the steam-bath with acetic anhydride (30 ml.) and pyridine (30 ml.). Removal of the

[40] Dickson, Page, and Rogers, *J.*, 1955, 443.
[41] Johnson, *J. Amer. Chem. Soc.*, 1951, **73**, 5888.

excess of acetylating mixture under reduced pressure and trituration of the residue with methanol then gave 3β-acetoxy-23*a*-bromo-11β-hydroxy-5α : 25*D*-spirostan-12-one (8·1 g., 18%) identical with the material described above.

The mother-liquors from the monoacetate were diluted with water, and the solid (8·3 g.), so obtained, was chromatographed on alumina (Peter Spence, Grade O; 200 g.). The material obtained by elution with benzene–light petroleum (3 : 1), benzene, and ether–benzene (1 : 9 and 1 : 4) was crystallised from benzene–light petroleum (b. p. 60—80°), to give 3β : 11β-*diacetoxy*-23a-*bromo*-5α : 25D-*spirostan*-12-*one* (2·8 g., 6%), m. p. 159—169°. Crystallisation from aqueous methanol raised the m. p. to 168—171°; $[\alpha]_D$ was +32° (*c* 1·4) (Found: C, 60·8; H, 7·5; Br, 12·9. $C_{31}H_{45}O_7Br$ requires C, 61·1; H, 7·4; Br, 13·1%), $\nu_{max.}$ (in CS_2) 1750 and 1218 (displaced OAc), 1735 and 1238 (OAc), 1720 (displaced CO), 1010, 945, 920, and 728 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

The *toluene*-p-*sulphonylhydrazone* was prepared as described above for the 3-monoacetate. Crystallised from aqueous acetone, it had m. p. 197—199°, $[\alpha]_D$ −150° (*c* 0·78) (Found: C, 58·9; H, 6·9. $C_{38}H_{53}O_8N_2BrS$ requires C, 58·7; H, 6·9%), $\lambda_{max.}$ (in EtOH) 226·5 mμ (ε = 12,700), $\nu_{max.}$ (in CS_2) 3200 (NH), 1720—1730 and 1238 (OAc), 1165 (SO_2·NH), 1016, 945, 918, and 732 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

(b) *From the 3-monoacetate.* A solution of 3β-acetoxy-23*a*-bromo-11β-hydroxy-5α : 25*D*-spirostan-12-one (200 mg.) in pyridine (2·5 ml.) and acetic anhydride (2·5 ml.) was left at room temperature for 7 days. The solution was poured on ice, and the solid (208 mg.) filtered off; it had $[\alpha]_D$ +27°. Crystallisation from benzene–light petroleum (b. p. 60—80°) gave 109 mg. of the diacetate, m. p. 169—173°, $[\alpha]_D$ +30°.

Lithium Aluminium Hydride Reduction of the 3-Mono- and 3 : 11-Di-acetates of 3β : 11β-*Dihydroxy*-23a-*bromo*-5α : 25D-*spirostan*-12-*one*.—Reduction of the diacetate (200 mg.) in boiling tetrahydrofuran (5 ml.) with lithium aluminium hydride (100 mg.) and isolation of the product with ether gave a crude product (155 mg.) that was debrominated by treatment with zinc dust (0·7 g.) in boiling acetic acid (5 ml.) for 2 hr. Hydrolysis with boiling 4% methanolic sodium hydroxide for 30 min. then gave a crude product (110 mg.), paper chromatography of which revealed the presence of 5α : 25*D*-spirostan-3β : 11β : 12β-triol but not that of the other 3β : 11 : 12-triols. Crystallisation of the material from aqueous methanol gave the 3β : 11β : 12β-triol (68 mg., 46%) as needles, m. p. 252—257°, $[\alpha]_D$ −66·5°, identified by its infrared spectrum with a sample prepared by the method of Djerassi *et al.*,[16] who give m. p. 262—263°, $[\alpha]_D$ −64°.

A similar reduction of the monoacetate with lithium aluminium hydride left some ketone unchanged, but retreatment with the reducing agent, followed by zinc debromination as described above, gave a crude material in 75% yield that was found, by paper chromatography, to contain 5α : 25*D*-spirostan-3β : 11β : 12β- and -3β : 11β : 12α-triol. Crystallisation from aqueous methanol gave a poor yield of needles, m. p. 248—252°, shown by infrared spectroscopy to consist essentially of the 3β : 11β : 12β-triol.

Action of Zinc upon 3β-*Acetoxy*-23a-*bromo*-11β-*hydroxy*-5α : 25D-*spirostan*-12-*one*.—The steroid (100 mg.) was boiled for 2 hr. with zinc dust (100 mg.) and acetic acid (2 ml.). After removal of excess of zinc and zinc salts, dilution with water gave a crude solid (69 mg.) whose infrared spectrum suggested that it consisted largely of 3β-acetoxy-12β-hydroxy-5α : 25*D*-spirostan-11-one (IV; R = Ac, X = H). Acetylation with acetic anhydride (1 ml.) and pyridine (1 ml.) overnight at room temperature and crystallisation from ethanol gave the corresponding diacetate (VIII; R = Ac) (20 mg.), m. p. 225—228°, identified by mixed m. p. and infrared spectrum with an authentic specimen.

Action of Zinc upon 3β : 11β-*Diacetoxy*-23a-*bromo*-5α : 25D-*spirostan*-12-*one*.—The steroid (200 mg.) was boiled for 4 hr. with zinc dust (2 g.) and acetic acid (6 ml.). The product, isolated as above in 88% yield, was somewhat impure hecogenin acetate, m. p. 225—239°, $[\alpha]_D$ −2·5°. Crystallisation from methanol gave the pure material, m. p. 242—246°.

Rearrangement of the Acetates of 23a-*Bromo*-3β : 11β-*dihydroxy*-5α : 25D-*spirostan*-12-*one*.—(a) *With sodium hydroxide in aqueous* tert.-*butyl alcohol.* The 3-monoacetate (200 mg.) was boiled for 6 hr. with 5% aqueous sodium hydroxide (5 ml.) and *tert.*-butyl alcohol (5 ml.). On removal of the alcohol by distillation, 23*a*-bromo-3β : 12β-dihydroxy-5α : 25*D*-spirostan-11-one (174 mg., 94%) separated {m. p. 214° (decomp.); $[\alpha]_D$ −33° (*c* 0·79)}. Treatment of 3β : 11β-diacetoxy-23*a*-bromo-5α : 25*D*-spirostan-12-one with alkali under the same conditions gave the 12β-hydroxy-11-ketone (VII; R = H), m. p. 214° (decomp.), $[\alpha]_D$ −33°, in 92% yield.

(b) *With alkali at room temperature.* The 3-monoacetate (250 mg.) was left at room temperature with a mixture of 2·5% aqueous potassium hydroxide (16·7 ml.) and dioxan (33·3 ml.).

The specific rotation of the solution, initially +5°, rose in 1½ hr. to +9° and then fell during *ca.* 70 hr. to a steady value of −28°. The 12β-hydroxy-11-ketone (VII; R = H), isolated in the usual way, had m. p. 210° (decomp.), $[\alpha]_D$ −32°.

(c) *With methanolic hydrochloric acid.* Treatment of the 3-monoacetate (0·5 g.) with boiling concentrated hydrochloric acid (2 ml.) and methanol (50 ml.) for 90 min. gave 0·35 g. of crude 12β-hydroxy-11-ketone (VII; R = H), m. p. 210° (decomp.), $[\alpha]_D$ −32°.

(d) *With acetic acid.* A solution of the monoacetate (100 mg.) in acetic acid (10 ml.) was heated at 100°. The specific rotation was initially +11·0° and fell in 6 hr. to a steady value of −23°. Precipitation with water then gave 80 mg. of 3β-acetoxy-23*a*-bromo-12β-hydroxy-5α : 25*D*-spirostan-11-one, m. p. 213° (decomp.), $[\alpha]_D$ −42° (*c* 0·65), identical with a sample prepared as described above.

23a-*Bromo*-5α : 25D-*spirostan*-3β : 11β : 12α-*triol* (XII; R = R′ = H, X = Br).—Trichloroacetic acid (55 g.) was dissolved in toluene and the solution was dried over calcium chloride for a few hours. The solution was filtered, 3β-acetoxy-23*a*-bromo-11β : 12β-epoxy-5α : 25*D*-spirostan [2] (50 g.) was added and the solution was diluted with toluene to about 1 l., left at room temperature for 3 days, then cooled to 0° and washed with cold sodium hydrogen carbonate solution and with water. The toluene solution was dried ($MgSO_4$) and evaporated to dryness. The residue was a glass, $\nu_{max.}$ (in CS_2) 3610 (OH), 1760 and 1240 (trichloroacetate), 1732 and 1240 (OAc), 1014, 948, 918, and 728 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

The crude trichloroacetate was boiled for 2 hr. with sodium hydroxide (100 g.) in water (100 ml.) and ethanol (1500 ml.). Most of the alcohol was removed by distillation and the residue was diluted with water. The suspension of solid was shaken with chloroform: it dissolved and, almost immediately, a crystalline hydrate separated which was filtered off and boiled with benzene in a flask fitted with a water separator and condenser. As water was removed, the solid went into solution. The solution was decolorized with charcoal, filtered, and allowed to cool: 23a-*bromo*-5α : 25D-*spirostan*-3β : 11β : 12α-*triol* (26·3 g., 55%) [m. p. 187—189° (decomp.)]. Crystallisation from benzene gave material of m. p. 190—192° (decomp.), $[\alpha]_D$ −26° (*c* 0·86). For analysis, a specimen was dried at 120°/0·1 mm. for 4 hr. (Found: C, 61·4; H, 8·6. $C_{27}H_{43}O_5Br$ requires C, 61·5; H, 8·2%) and had $\nu_{max.}$ (in Nujol) 3620 and 3430 (OH), 1016, 951, 914, and 722 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

An experiment in which the time of reaction of epoxide with trichloroacetic acid was extended to 7 days gave a 54% yield of the triol.

3β : 12α-*Diacetoxy*-23a-*bromo*-5α : 25D-*spirostan*-11β-*ol* (XII; R = R′ = Ac, X = Br).—The above triol (5 g.) was shaken at room temperature with pyridine (50 ml.) and acetic anhydride (50 ml.) for 16 hr., during which the solid dissolved. The mixture was distilled to dryness under reduced pressure and the last trace of acetylating mixture removed by refluxing the residual gum for 15 min. with methanol and again evaporating. Crystallisation of the residue from a little methanol gave the *diacetate* (3·04 g.), m. p. 195—198° (decomp.), and a second crop (1·89 g.), m. p. 194—196° (decomp.) (total yield 85%). Purification by chromatography and crystallisation from methanol gave needles, m. p. 201—203° (decomp.), $[\alpha]_D$ −23·4° (*c* 1·6) (Found: C, 60·7; H, 7·85. $C_{31}H_{47}O_7Br$ requires C, 60·9; H, 7·75%), $\nu_{max.}$ (in CS_2) 3620 and 3550 (OH), 1738 and 1236 (OAc), 1024, 944, 914, and 722 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

3β : 12α-*Diacetoxy*-23a-*bromo*-5α : 25D-*spirostan*-11-*one* (XIII; R = Ac, X = Br).—Chromic anhydride (flake; 2·4 g.) was added to pyridine (40 ml.) with stirring and water-cooling. When formation of the complex was complete (*ca.* 1 hr.) a solution of 3β : 12α-diacetoxy-23*a*-bromo-5α : 25*D*-spirostan-11β-ol (3·0 g.) in pyridine (30 ml.) was added and the mixture was stirred for 4 hr. An equal volume of benzene was added and the mixture was filtered. The residue was washed with cold benzene, and the combined filtrate and washings were washed successively with water, 2N-hydrochloric acid, sodium hydrogen carbonate solution, and water. The solution was dried ($MgSO_4$) and evaporated. Crystallisation of the residual gum from methanol gave the *ketol diacetate* (2·26 g., 76%), m. p. 164—166°. Further crystallisation from the same solvent raised the m. p. to 168—171°; $[\alpha]_D$ was +7·2° (*c* 1·27) (Found: C, 61·3; H, 7·3. $C_{31}H_{45}O_7Br$ requires C, 61·1; H, 7·4%). Infrared spectrum: see ref. 13.

23a-*Bromo*-3β : 12α-*dihydroxy*-5α : 25D-*spirostan*-11-*one* (XIII; R = H, X = Br).—The foregoing diacetate (0·25 g.) in ethanol (25 ml.) was treated with a solution of potassium hydroxide (1·25 g.) in the minimum volume of water, and the solution was left overnight at room temperature, then poured into water. A solid separated which was filtered off, washed with water, and dried. Crystallisation from acetone gave the *ketol* as needles, m. p. 209—211° (decomp.), $[\alpha]_D$ −7·7° (*c* 0·83) (Found: C, 61·5; H, 7·9. $C_{27}H_{41}O_5Br$ requires C, 61·7; H,

7·9%), $\nu_{max.}$ (in Nujol) 3620 and 3430 (OH), 1695 (CO), 1008, 942, 918, and 720 cm.$^{-1}$ (23*a*-bromo-25*D*-spirostan).

The m. p. of this material depended greatly on the rate of heating and apparently on the solvent used for crystallisation.

The ketol did not reduce Fehling's solution.

Reacetylation of the ketol with pyridine and acetic anhydride, overnight at room temperature, gave the original diacetate (XIII; R = Ac, X = Br).

5α : 25D-*Spirostan*-3β : 11β : 12α-*triol* (XII; R = X = H).—23*a*-Bromo-5α : 25*D*-spirostan-3β : 11β : 12α-triol (20 g.), zinc dust (acid washed; 100 g.), and acetic acid (200 ml.) were boiled together with stirring for 2 hr. The solution was filtered and the residue was washed with boiling acetic acid. The combined filtrate and washings were evaporated to small bulk under reduced pressure and diluted with water. The solid was filtered off, washed with water, and dried. This partially acetylated material was hydrolysed with a boiling mixture of 40% aqueous sodium hydroxide (40 ml.) and ethanol (400 ml.) for 2 hr. Most of the solvent was distilled off and the residue was diluted with water. The precipitated solid crystallised from aqueous methanol (charcoal) in two crops, giving 13·37 g. (79%) of material, m. p. 247—251°. Crystallisation from acetonitrile gave the pure *triol*, m. p. 250—254°, $[\alpha]_D$ −33° (*c* 0·85) (Found: C, 72·4; H, 10·0. $C_{27}H_{44}O_5$ requires C, 72·3; H, 9·9%), $\nu_{max.}$ (in Nujol) 3430 (OH), 979, 920, 898, and 861 cm.$^{-1}$ (25*D*-spirostan).

3β : 12α-*Diacetoxy*-5α : 25D-*spirostan*-11β-*ol* (XII; R = Ac, X = H).—The foregoing triol (11·64 g.) was shaken overnight at room temperature with pyridine (116 ml.) and acetic anhydride (116 ml.). The product was worked up as in the preparation of the 23-bromo-compound. Crystallisation from methanol gave 11·49 g. (83%) of material, m. p. 235—238°. Further crystallisation from aqueous dioxan gave the *diacetate*, m. p. 239—241°, $[\alpha]_D$ −29° (*c* 0·87) (Found: C, 69·95; H, 9·1. $C_{31}H_{48}O_7$ requires C, 69·9; H, 9·1%), $\nu_{max.}$ (in CS_2) 3620 and 3550 (OH), 1732—1722 and 1240—1230 (acetates), 978, 918, 895, and 862 cm.$^{-1}$ (25*D*-spirostan).

3β : 12α-*Diacetoxy*-5α : 25D-*spirostan*-11-*one* (XIII; R = Ac, X = H).—The oxidation was carried out as described above for the 23-bromo-derivative with the foregoing triol diacetate (10 g.) in pyridine (120 ml.) added to the complex prepared from chromic anhydride (9·5 g.) and pyridine (160 ml.). Crystallisation from methanol gave 7·12 g., m. p. 186—190°, and a second crop (1·30 g.), m. p. 181—185° (total yield 84·5%). Further crystallisation from methanol gave the *ketol diacetate* as needles, m. p. 188—190°, $[\alpha]_D$ +5·3° (*c* 0·94) (Found: C, 70·4; H, 8·5. $C_{31}H_{46}O_7$ requires C, 70·15; H, 8·7%), $\nu_{max.}$ (in CS_2) 1756 and 1218 (displaced OAc), 1735 and 1238 (OAc), 1735 (displaced CO), 978, 918, and 895 cm.$^{-1}$ (25*D*-spirostan).

3β : 12α-*Dihydroxy*-5α : 25D-*spirostan*-11-*one* (XIII; R = X = H).—The diacetate (4·5 g.) was hydrolysed with potassium hydroxide (22·5 g.) in aqueous ethanol (450 ml.) as described for the preparation of the 23-bromo-analogue. The *ketol* (3·54 g., 93%) separated from aqueous acetone as crystals, m. p. 257—258°. Further crystallisation from aqueous acetone gave material, m. p. 250—255°, $[\alpha]_D$ −13·2° (*c* 1·17). For analysis it was dried in a high vacuum at 140° (Found: C, 72·5; H, 9·8. $C_{27}H_{42}O_5$ requires C, 72·6; H, 9·5%), $\nu_{max.}$ (in Nujol) 3400 (OH), 1703 (CO), 976, 918, 895, and 865 cm.$^{-1}$ (25*D*-spirostan).

Crystallisation from methanol appeared to give a different form which, even after being heated at 140° *in vacuo*, was solvated. It melted at 251—255° (Found: C, 71·25; H, 9·45. $C_{27}H_{42}O_5,\frac{1}{2}$MeOH requires C, 71·4; H, 9·6%), and had $\nu_{max.}$ (in Nujol) 3400 (OH), 1694 and 1708 (CO), 980, 920, 892 and 865 cm.$^{-1}$ (25*D*-spirostan). When dissolved in chloroform, the two forms had identical spectra, except as due to the presence of methanol in the solvated form. The splitting of the carbonyl stretching band in the Nujol spectrum of the solvated form is attributed to intermolecular hydrogen bonding.

The ketol did not reduce Fehling's solution. Reacetylation at room temperature overnight with pyridine and acetic anhydride gave the diacetate (XIII; R = Ac, X = H).

Debromination of 3β : 12α-*Diacetoxy*-23a-*bromo*-5α : 25D-*spirostan*-11-*one*.—The ketol diacetate (250 mg.) was boiled for 2 hr. with zinc dust (acid-washed; 1 g.) and acetic acid (2·5 ml.). The crude product (210 mg.), isolated in the usual way, had m. p. 168—174°, $[\alpha]_D$ +3°. The infrared spectrum was virtually identical with that of an authentic specimen of (XIII; R = Ac, X = H). Crystallisation from methanol gave 120 mg. of material with m. p. 180—183°.

Action of Alkali upon 3β : 12α-*Dihydroxy*-5α : 25D-*spirostan*-11-*one and its Diacetate*.—(a) *Sodium hydroxide in aqueous* tert.-*butyl alcohol*. Treatment of the diacetate with a boiling mixture of 1·25N-aqueous sodium hydroxide and an equal volume of *tert.*-butyl alcohol for 6 hr. merely caused hydrolysis of the ester groupings. The crude product had m. p. 240—250° and $[\alpha]_D$ −12·5°; reacetylation gave the original diacetate, m. p. 178—194°, $[\alpha]_D$ +4°.

(b) *Potassium hydroxide in aqueous dioxan.* Treatment of the diacetate with equal volumes of 0·9N-aqueous potassium hydroxide and dioxan at the b. p. for 6 hr. gave a crude dihydroxy-ketone with $[\alpha]_D$ −26°, corresponding to a 50% conversion into the 12β-epimer (it being assumed that no other change occurred simultaneously); after 24 hours' treatment the crude product had $[\alpha]_D$ −33° and acetylation gave a crude diacetate, m. p. 204—211°, $[\alpha]_D$ −64° (corresponding to 82% epimerisation). Crystallisation of this material gave 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one (VIII; R = Ac) (about 50%), m. p. 221—225°, $[\alpha]_D$ −77°, infrared spectrum identical with that of authentic material.

(c) *With alcoholic sodium hydroxide.* Treatment of the diacetate with 4N-sodium hydroxide in boiling 85% ethanol for 2 hr. and reacetylation gave material with $[\alpha]_D$ −64° (82% epimerisation); material obtained similarly after 6 hours' refluxing had $[\alpha]_D$ −69° (88% epimerisation). The crude dihydroxy-ketone obtained by 6 hours' hydrolysis of the diacetate (250 mg.) was treated in the usual way with Girard reagent P. From the "ketonic fraction" only 10 mg. of a gum were isolated; the non-reactive fraction was acetylated in the usual way and the product was crystallised from ethanol, to give 3β : 12β-diacetoxy-5α : 25*D*-spirostan-11-one (VIII; R = Ac) (184 mg., 74%), m. p. 223—226°, $[\alpha]_D$ −78·5°. Hydrolysis of the crystallisation residues and paper chromatography [cf. 24] showed the presence of the ketone (VIII; R = H), of a substance with an R_F value close to that of the α-hydroxy-epimer (XIII; R = X = H), and of a much more polar compound, probably a triol.

5α : 25D-*Spirostan*-3β : 11α : 12α-*triol* (XIV; R = H).—A solution of 3β-acetoxy-5α : 25*D*-spirost-11-en [42] (2·0 g.) in ether (125 ml.) containing pyridine (1 ml.) was treated with osmium tetroxide (1·0 g.) in ether (25 ml.). The mixture was left overnight and the osmium complex was filtered off, washed with ether, and boiled under reflux for 4½ hr. with sodium sulphite (18 g.) in ethanol (160 ml.) and water (80 ml.). The cooled mixture was filtered and the solid washed with boiling ethanol. The combined filtrate and washings were evaporated to small bulk under reduced pressure. Dilution of the residue with water gave the crude triol (1·48 g., 75%), m. p. 220—230°. After recrystallisation from aqueous ethanol or ethyl acetate–light petroleum, the substance had m. p. 226—228°, $[\alpha]_D$ −61° (*c* 1·7), $\nu_{max.}$ (in Nujol) 3400 (OH), 980, 918, 898, and 862 cm.$^{-1}$ (25*D*-spirostan). Hirschmann *et al.*[23] give m. p. 221—225°.

Acetylation of the triol with equal volumes of acetic anhydride and pyridine at 100° for 75 min. gave the *triacetate*, which was difficult to purify. Addition of water to a cold ethanolic solution gave it as a solid, m. p. 115—125°, $[\alpha]_D$ −49° (*c* 1) (Found: C, 69·1; H, 8·7. $C_{33}H_{50}O_8$ requires C, 69·0; H, 8·8%), $\nu_{max.}$ (in CS_2) 1738 and 1240 (OAc), 980, 920, 898, and 862 cm.$^{-1}$ (25*D*-spirostan).

Acknowledgment is made to Mr. W. F. Wall for assistance in the experimental work.

GLAXO LABORATORIES, LTD., GREENFORD, MIDDLESEX. [*Received, May 14th*, 1956.]

[42] Elks, Phillipps, Taylor, and Wyman, *J.*, 1954, 1739.