Studies in the Synthesis of Cortisone. Part VIII. A Wagner–Meerwein Rearrangement involving Rings C and D of the Steroid Nucleus.*

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Decomposition of hecogenin acetate toluene-*p*-sulphonylhydrazone with alkali gives little 3β-acetoxy-5α : 22a-spirost-11-en † (II); most of the steroid undergoes Wagner–Meerwein rearrangement, to give a small quantity of the known C-nor-D-homo-compound (V) and, as major product, a compound (A), which is considered to be (VII) or, less probably, (VI). These two rearranged products also arise from 3β-acetoxy-12β-methanesulphonyloxy-5α : 22a-spirostan (IV; R = Ac) by methanolysis. The structure of compound A is discussed in the light of both its reactions and the stereochemical requirements of the rearrangement.

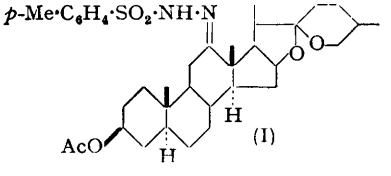
An attempt to prepare 5α : 22a-spirost-11-en-3-one (XVI) *via* 12α-hydroxy-5α : 22a-spirostan-3-one (XV; R = H) was unsuccessful, but 3β-acetoxy-5α : 22a-spirost-11-en (II) was readily obtained by the action of zinc upon 3β-acetoxy-12α : 23-dibromo-5α : 22a-spirostan-11β-ol (XIX). The structure of (II) was proved by its conversion, *via* the 11α : 12α-epoxide, into 3β : 12α-diacetoxy-5α : 22a-spirostan (XII; R = Ac).

The use of Δ^{11}-compounds derived from bile acids as intermediates in the partial synthesis of 11-keto-steroids is well known (see Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, 3rd Ed., pp. 452 *et seq.*), but the method has not been applied in the steroid sapogenin series, possibly for lack of a convenient method of preparing the Δ^{11}-compounds. Bamford and Stevens (*J.*, 1952, 4735) have, however, recently shown that the toluene-*p*-sulphonylhydrazones of aliphatic and alicyclic ketones can be converted into olefins by treatment with alkali:

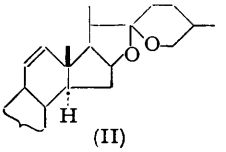
$$R{\cdot}CH_2{\cdot}CR'{:}N{\cdot}NHTos \xrightarrow{NaOH} R{\cdot}CH{:}CHR' + N_2 + TosONa \quad (Tos = p\text{-}C_6H_4Me{\cdot}SO_2)$$

the reaction is sometimes attended by rearrangement of the carbon skeleton (see below). This observation opened a possible route from hecogenin to 3β-acetoxy-5α : 22a-spirost-11-en (II) and hence to 11-oxotigogenin acetate; methods are already known for the conversion of the last-mentioned compound into cortisone.

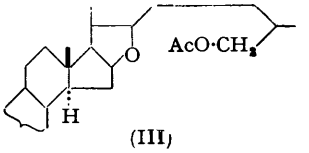
Hecogenin acetate reacted with toluene-*p*-sulphonhydrazide very slowly in boiling ethanol, but much faster in the presence of hydrochloric acid or in glacial acetic acid. Treatment of



(I)



(II)



(III)

the resulting toluene-*p*-sulphonylhydrazone (I) with caustic alkali in diethylene glycol at 130—140° or in boiling *n*-butanol or *n*-propanol produced mixtures from which three pure compounds were isolated. These compounds, which will be called A, B, and C (these letters refer to the acetates, unless otherwise specified), were obtained in yields of 50—55, <5, and up to 25% respectively.

Compound A had the correct elementary analysis for the required Δ^{11}-compound (II),

* Part VII, *J.*, 1954, 747.

† Scheer, Kostic, and Mosettig (*J. Amer. Chem. Soc.*, 1953, **75**, 4871) have shown that sarsasapogenin and smilagenin differ in their configurations at $C_{(25)}$ and possibly not, as earlier thought, at $C_{(22)}$. Although this finding casts some doubt on the nature of the isomerism of other sapogenins, we propose, in the absence of definite information on this point, to use the conventional name "22a-spirostan" for compounds derived from hecogenin. James (*Chem. and Ind.*, 1953, 1388) has very recently shown that hecogenin and smilagenin have the same configuration at $C_{(25)}$.

and its rotation (−57°) agreed with that (−66°) calculated from the rotation of tigogenin acetate and the contribution of an 11 : 12-double bond. The presence of a double bond was shown by the tetranitromethane test and by the formation of a very unstable crystalline dibromide. Doubt was cast upon structure (II) for compound A when an attempt was made to obtain tigogenin acetate from it by hydrogenation in presence of Adams catalyst. After 1 mol. of hydrogen had been taken up, the product was seen, from its infra-red absorption, to have undergone partial disruption of the side-chain. An attempt to complete this process by carrying the reduction to a total uptake of 2 mols. of hydrogen gave a mixture from which no pure compound could be isolated, whereas tigogenin acetate readily yielded 3β : 26-diacetoxy-5α : 22a-furostan (III) by reduction under similar conditions and subsequent acetylation.

Compound A reacted readily with 1 mol. of monoperphthalic acid to give two isomeric compounds, which from their analyses and infra-red spectra appeared to be epoxides. These two, " epoxide P " and " epoxide Q," were isolated in a ratio of *ca.* 1 : 2. If these had been isomeric 11 : 12-epoxides derived from (II), then lithium aluminium hydride should have converted one of them (the 11α : 12α-epoxide) into 12α-hydroxytigogenin and the other (11β : 12β-epoxide) into 11β-hydroxytigogenin (cf. Barton, *J.*, 1953, 1027; Fürst and Scotoni, *Helv. Chim. Acta*, 1953, **36**, 1332, 1410). Both epoxides were rather resistant to reduction with lithium aluminium hydride, but under sufficiently vigorous conditions gave diols which with pyridine and acetic anhydride at 100° yielded only monoacetates. The failure of the newly formed hydroxy-groups to undergo acetylation showed that neither of the diols was 12α-hydroxytigogenin and the physical properties of both monoacetates differed from those of the known 11β-hydroxytigogenin 3-monoacetate (Djerassi, Batres, Velasco, and Rosenkranz, *J. Amer. Chem. Soc.*, 1952, **74**, 1712). Further, the diol monoacetates were oxidised only slowly by chromic acid and the sole isolatable product, in each instance, was unchanged starting material.

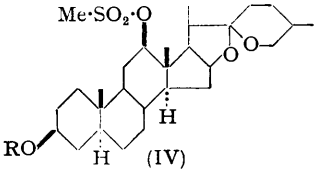
These experiments not only showed that the epoxides were not those derived from (II) but also suggested strongly that the double bond in compound A was ditertiary, since reduction with lithium aluminium hydride of the isomeric epoxides derived from such a compound would give isomeric (but not epimeric) tertiary alcohols (cf. Barton, *loc. cit.*). This was supported by the fact that the triol resulting from the action of osmium tetroxide upon compound A yielded only a monoacetate with acetic anhydride and pyridine at 100°.

In order to accommodate a ditertiary double bond in compound A, it is necessary to postulate a rearrangement of the carbon skeleton during decomposition of (I), if extremely improbable double bond shifts are excluded. Now it has already been mentioned that such rearrangements are liable to occur; camphor toluene-*p*-sulphonylhydrazone, for example, undergoes Wagner–Meerwein rearrangement during decomposition with alkali and gives camphene (Bamford and Stevens, *loc. cit.*); further, Hirschmann, Snoddy, and Wendler (*J. Amer. Chem. Soc.*, 1952, **74**, 2693) have shown that solvolysis of the rockogenin derivative (IV; R = $MeO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CO$) was accompanied by rearrangement and yielded a product that they formulated as (V).* This compound was clearly a possible product of our reaction, and in fact, the minor product B had physical properties agreeing with those quoted for (V; R = Ac). In order to obtain an authentic specimen of (V; R = Ac), 3β-acetoxy-12β-methanesulphonyloxy-5α : 22a-spirostan (IV; R = Ac) was prepared by reduction of hecogenin acetate with sodium borohydride and treatment of the product with methanesulphonyl chloride in pyridine. When the crude (IV; R = Ac), which contained some of the 12α-epimer, was boiled in methanol and the product reacetylated, the major product was compound A, the expected (V; R = Ac) being isolated in very small quantity. (The 12α-methanesulphonyloxy-compound was recovered unchanged : it was found to be stable to prolonged boiling with methanol and was recovered after alkaline hydrolysis and re-acetylation of the amorphous 3-hydroxy-compound; cf. Hirschmann *et al.*, *loc. cit.*).

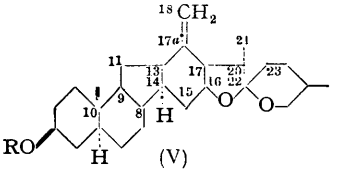
It is known that the Wagner–Meerwein rearrangement occurs most readily (or, in some

* We refrain from naming this ring system at present but, if essential, names of the type 3β-hydroxy-c-nor-D-homo-5α : 22a-spirost-17a-en (for V, R = H) would be used, with numbering as shown for (V) (cf. Fried and Klingsberg, *J. Amer. Chem. Soc.*, 1953, **75**, 4929; Hiskey, Hirschmann, and Wendler, *ibid.*, p. 5135). No assumptions are at present made about the stereochemistry at $C_{(13)}$.

instances, only) when the four reacting centres lie in a plane (cf. Barton, *loc. cit.*). In (IV) the $C_{(12)}$–O bond is β-orientated (equatorial) and the condition of co-planarity is satisfied by the chains $O–C_{(12)}–C_{(13)}–C_{(14)}$ and $O–C_{(12)}–C_{(11)}–C_{(9)}$; in the 12α-epimer (polar) of (IV) there are no similar sets of co-planar centres and, as Hirschmann *et al.* (*loc. cit.*) have shown and we have confirmed, the 12α-methanesulphonyloxy-compounds are not affected by the conditions causing rearrangement in (IV). (Analogous compounds in the bile acid series are known to undergo simple elimination under more vigorous conditions with formation of an 11 : 12-double bond; the co-planar atoms in this instance are $O–C_{(12)}–C_{(11)}–11β$-H.)



(IV)



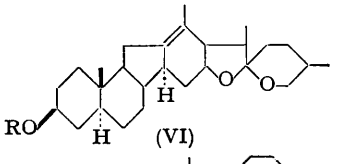
(V)

In the decomposition of (I), it is probable that a double-bond rearrangement of the following type occurs under the influence of base and that it is the azo-form (which may well exist only transitorily) that undergoes decomposition and rearrangement through the conventional carbonium-ion intermediates (cf. Wheland, " Advanced Organic Chemistry," John Wiley & Sons, Inc., New York, 2nd Ed.; Ingold, *J.*, 1953, 2845):

A double-bond migration of similar type is believed to occur during the Wolff–Kishner and related reactions; see Seibert, *Chem. Ber.*, 1947, **80**, 494; Todd, *J. Amer. Chem. Soc.*, 1949, **71**, 1356; Barton, Holness, and Klyne, *J.*, 1949, 2456; Beech, Turnbull, and Wilson, *J.*, 1952, 4686.

In such a double-bond rearrangement the newly formed single bond between $C_{(12)}$ and N will be predominantly in the more stable equatorial (*i.e.*, β-)configuration and the geometrical factors will be similar to those obtaining in (IV). The formation of some Δ^{11}-compound during the decomposition of (I) (see below) suggests that a proportion of the azo-intermediate has the $C_{(12)}$–N bond in the polar (α) configuration, which would be suitably disposed for involvement of the 11β-hydrogen atom.

It has already been mentioned that a β-bond at $C_{(12)}$ is coplanar both with atoms $C_{(13)}$ and $C_{(14)}$ and with atoms $C_{(11)}$ and $C_{(9)}$. If the first of these co-planar sets is involved in the rearrangement, then any of the compounds (V), (VI), and (VII) might be formed. Formula



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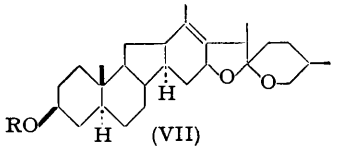
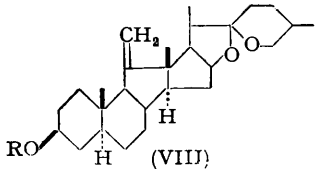
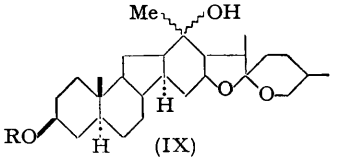


(VII)



(VIII)

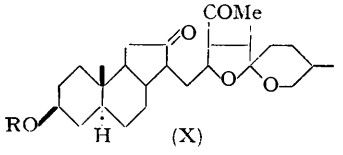


(IX)

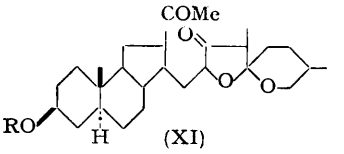
(V) has already been put forward for compound B (and the presence of an exocyclic methylene group was demonstrated conclusively by Hirschmann *et al.*, *loc. cit.*), and either of the formulæ (VI) and (VII) would account for the properties of compound A. On the other hand, rearrangement involving the second of the above sets of coplanar atoms could

give rise only to structure (VIII), which would account for the properties neither of compound A nor of compound B. [Compound B is not to be represented by formula (VIII), because the ketone derived from it by cleavage of the exocyclic double bond shows a peak in the infra-red at 1712 cm.$^{-1}$ (Hirschmann *et al.*, *loc. cit.*), whereas (VIII) would give a 5-membered ring ketone with carbonyl absorption at *ca.* 1740 cm.$^{-1}$.] A further argument against this second mode of rearrangement is that it would involve a primary carbonium ion, which would be less favoured, on grounds of stability, than the tertiary carbonium ion involved in the alternative scheme.

We consider, therefore, in agreement with the American workers, that compound B has formula (V) and, further, that compound A is either (VI) or (VII). An attempt to obtain



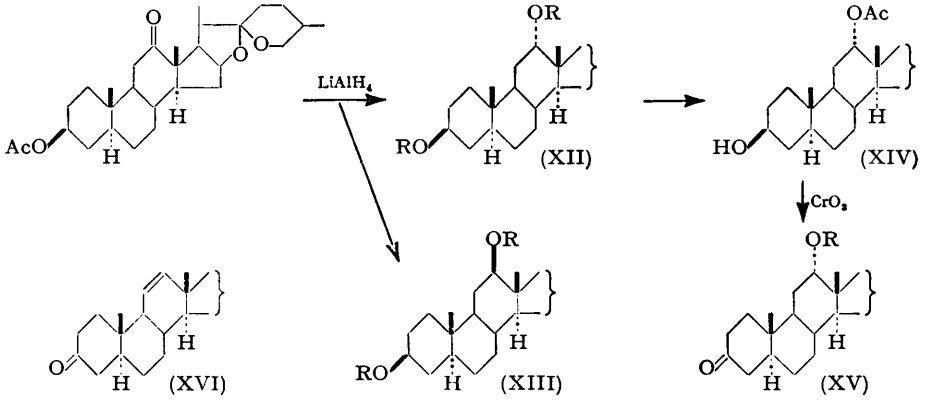
(X)



(XI)

direct evidence of such a close inter-relation was, unfortunately, inconclusive. Whether compound A has structure (VI) or (VII), one of the two isomeric epoxides, P and Q, should, on reduction with lithium aluminium hydride, give the tertiary alcohol (IX), and this might, in turn, be expected to yield (V) on dehydration. However, phosphorus oxychloride treatment, in cold pyridine, of the monoacetate of either diol resulting from reduction of the epoxides P and Q yielded only compound A, and infra-red analysis showed that (V) was not formed in significant amount.

The available evidence is insufficient to allow a clear choice between structures (VI) and (VII), but some support for structure (VII) comes from results of periodate fission of the triol obtained from compound A with osmium tetroxide. The product of this reaction was a diketone, which was shown by the nitroprusside test to be a methyl ketone; its infra-red spectrum showed bands at 1714 cm.$^{-1}$, corresponding to a normal ketone, and at 1740 cm.$^{-1}$,



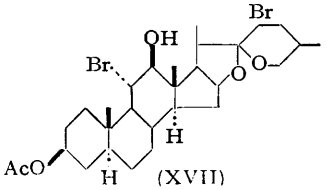
corresponding to a 5-membered ring ketone. These results would agree with either of the postulated structures for compound A, since the products from (VI) and (VII) would be (X) and (XI) respectively. However, compound (XI), which is a potential α-ketol, might be expected to show reducing properties, whereas there is no obvious reason why (X) should do so. In fact, the diketone did give a weak positive test with Fehling's solution, suggesting that it had structure (XI) and that compound A is to be represented by (VII).

Along with the work described above, the synthesis of Δ^{11}-compounds by unambiguous methods was investigated. First, an attempt was made to prepare 5α : 22a-spirost-11-en-3-one (XVI) by the method shown, for comparison with the product of chromic oxidation of compound A (free alcohol).

Hecogenin acetate was reduced with lithium aluminium hydride (Hirschmann *et al.*, *loc. cit.*) and, after acetylation, the rockogenin diacetate (XIII; R = Ac) was separated from

its 12α-epimer (XII; R = Ac) by chromatography. The 12α-acetoxy-compound (XII; R = Ac), on treatment with potassium hydrogen carbonate in boiling aqueous methanol, gave the 12-monoacetate (XIV) (12α-acetoxy-groups are known to be rather resistant to hydrolysis; see Koechlin and Reichstein, *Helv. Chim. Acta*, 1942, **25**, 918), and oxidation of the latter compound with chromic acid gave the 3-keto-steroid (XV; R = Ac). Both the free alcohol (XV; R = H) and the benzoate (XV; R = Bz) were prepared and heated under water-pump pressure, but each compound sublimed unchanged. Lack of material prevented further investigation of the reaction.

Cornforth and Osbond (*Chem. and Ind.*, 1953, 919) have shown that the mixture of bromohydrins (XVII) and XVIII), obtained by reduction of 11α : 23-dibromohecogenin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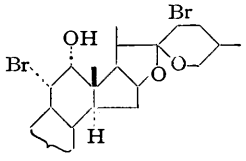
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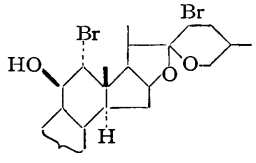
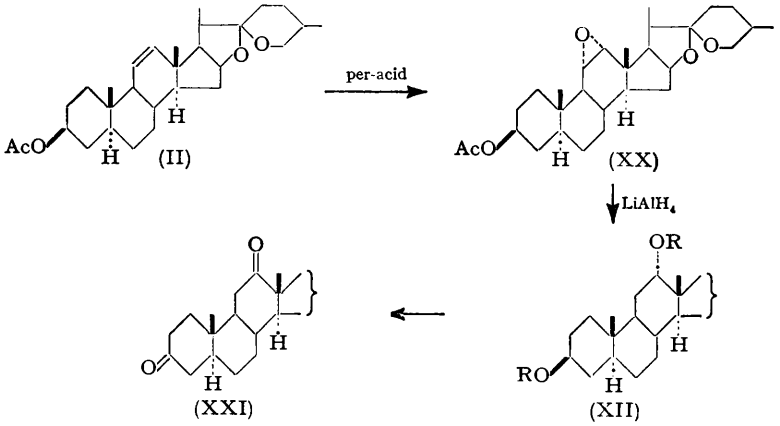

(XIX)

acetate with sodium borohydride, is reduced with zinc in acetic acid to a compound formulated as 3β-acetoxy-23-bromo-5α : 22a-spirost-11-en, but we have found some difficulty in obtaining the pure bromine-free compound (II) by this reaction under more vigorous conditions. It seemed probable that this elimination reaction would proceed most readily if both the bromine and the hydroxy-groups were polar (cf. Barton and Rosenfelder, *J.*, 1951, 1048; Barton, *Experientia*, 1950, **6**, 316) as in the bromohydrin (XIX) (Cornforth and Osbond, *loc. cit.*) and, in fact, (XIX) reacted with zinc in boiling acetic acid to give, in high yield, a compound with the correct analysis for 3β-acetoxy-5α : 22a-spirost-11-en (II). There was initially some doubt about the structure of the reduction product, since it gave only a very weak tetranitromethane test, but it was proved to be (II) by the following



(II) (XX) (XXI) (XII)

reactions. With monoperphthalic acid it gave a single compound, which, by analogy with the epoxidation of Δ^{11}-compounds in the bile acid series, must be the 11α : 12α-epoxide (XX) (Gallagher and Long, *J. Biol. Chem.*, 1946, **162**, 495; McKenzie, McGuckin, and Kendall, *ibid.*, p. 555; Press and Reichstein, *Helv. Chim. Acta*, 1942, **25**, 878; Berner and Reichstein, *ibid.*, 1946, **29**, 1374). Vigorous reduction of the epoxide with lithium aluminium hydride in boiling tetrahydrofuran gave 5α : 22a-spirostan-3β : 12α-diol (XII; R = H), which was characterized as its diacetate and by chromic oxidation to hecogenone (XXI).

With the synthesis of (II), the structure of the third product formed from (I) by decomposition with alkali became clear, since compound C was found, by comparison of its physical properties and infra-red spectrum with those of an authentic specimen, to be the desired Δ^{11}-compound (II). The yield of this compound from (I) was, however, too low for the method to be of any interest in a practicable synthesis of cortisone.

Addendum.—Since this manuscript was prepared, Hiskey, Hirschmann, and Wendler (*J. Amer. Chem. Soc.*, 1953, **75**, 5135) have briefly reported both the preparation of compound A from hecogenin toluene-*p*-sulphonylhydrazone and the oxidation of the olefin with osmium tetroxide. They assign to compound A the alternative structures (VI) and (VII) and show that it can be obtained from (V) by treatment with formic acid at room temperature; this observation supports the relation between compounds A and B that we have put forward.

In view of this ready conversion of compound B into compound A with acid, it seemed possible that our failure to obtain B in significant quantity by methanolysis of (IV; R = Ac) was a consequence of double-bond migration induced by acid present in the crude (IV) employed or by the methanesulphonic acid liberated during the reaction. We have now found that, if (IV; R = Ac) is treated with potassium *tert.*-butoxide in *tert.*-butanol, a high yield of B is, in fact, obtained, but, surprisingly, compound B was not affected by treatment either with methanesulphonyl chloride or with toluene-*p*-sulphonic acid in boiling chloroform–methanol. Subsequent experiments confirmed that the nature of the solvent is more important in determining the yield of B than is the presence or absence of base.

Experimental

Rotations were determined on chloroform solutions (*ca.* 1%) unless otherwise stated. M. p.s were taken on a Kofler block. A Perkin–Elmer model 21 double-beam spectrophotometer equipped with rock-salt optics was used for the determination of infra-red spectra.

Hecogenin Acetate Toluene-p-*sulphonylhydrazone* (I).—(*a*) Hecogenin acetate (100 g.), toluene-*p*-sulphonhydrazide (100 g.), and anhydrous ethanol (7 l.) were boiled together under reflux for 65 hr. The mixture was allowed to cool somewhat and the solid (100 g., 74%) was then filtered off, washed with a little ethanol, and dried. This material, which melted at 268—269°, was suitable for use in the next stage. Crystallisation from a mixture of ethanol and chloroform gave the *hydrazone* as fine needles, m. p. 274° (decomp.), $[\alpha]_D$ −15° (Found: C, 67·1; H, 8·1; N, 4·5; S, 5·0. $C_{36}H_{52}O_6N_2S$ requires C, 67·5; H, 8·2; N, 4·4; S, 5·0%), $\lambda_{max.}$ (in EtOH) 226 mμ (ε = 11,600), ν_{max} (in CS_2) 3250 (imine), 1732 and 1245 (acetate), 1342 and 1160 (monosubstituted sulphonamide), 977, 914, 897, and 860 (22a-spirostan) (C.S. no. 112).*

In another experiment, with 36 g. of hecogenin acetate, 18·6, 24·9, and 31·1 g. of derivative were deposited after 6, 24, and 50 hr. respectively.

(*b*) A solution of hecogenin acetate (20 g.) in chloroform (150 ml.) was added to toluene-*p*-sulphonhydrazide (10 g.) in a mixture of ethanol (200 ml.) and concentrated hydrochloric acid (5 ml.); crystalline solid began to separate within a few minutes. After being left overnight the hydrazone (23 g., 85%) was filtered off, washed with methanol, and dried; it had m. p. 278—280° (decomp.).

(*c*) Hecogenin acetate (2 g.) was dissolved in warm acetic acid (60 ml.), the solution was cooled, and toluene-*p*-sulphonhydrazide (2 g.) was added with shaking. After about 5 min., solid began to separate, and after an hour this solid was filtered off and washed with ethanol. The product (2·4 g., 89%) melted at 264—265° (decomp.) and had $[\alpha]_D$ −14·9°.

Alkaline Decomposition of Hecogenin Acetate Toluene-p-*sulphonylhydrazone.*—(*a*) Sodium (15 g.) was dissolved in diethylene glycol (1 l.) with warming, the solution was cooled to about 50°, and the hydrazone (50 g.) was added. The mixture was then heated gradually to 130—140° and kept at that temperature until no further gas evolution was apparent. After being cooled to about 60°, the mixture was diluted with much water and kept overnight at room temperature. The solid was filtered off, washed with water, and dried in a desiccator. This crude product (35 g.), which had no definite m. p., was crystallised twice from boiling acetonitrile. The resulting "compound A" (free alcohol) (21·4 g.), which appeared to be solvated, melted indefinitely between 125° and 133° after preliminary softening. This material was acetylated on the water-bath for 30 min. with acetic anhydride (215 ml.) and pyridine (215 ml.). The solution was evaporated to dryness, the remaining acetic anhydride was removed by repeated evaporation with methanol, and the residue was crystallised from methanol. The "compound A" (19·5 g., 55%), so obtained, melted at 141—144°. Further crystallisation from aqueous methanol gave material melting at 142—145°, $[\alpha]_D$ —57° (Found: C, 76·55; H, 9·65. Calc. for

* Infra-red spectra thus marked have been deposited with the Society. Photo-copies (price, 3*s.* 0*d.* each per copy) can be obtained on application, quoting the C.S. no., to the General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1.

$C_{29}H_{44}O_4$: C, 76·3; H, 9·7%), $\nu_{max.}$ (in CS_2) 1733 and 1238 (acetate), 980, 920, 898 and 860 (22a-spirostan). Hiskey *et al.* (*loc. cit.*) give m. p. 142—144°, $[\alpha]_D$ —52·6° in $CHCl_3$.

The free *alcohol*, prepared as above, or by hydrolysis of the acetate with alcoholic potassium hydroxide, had m. p. 120—125° and $[\alpha]_D$ −55° (Found, after drying at 100°/0·01 mm.: C, 78·4; H, 10·25. $C_{27}H_{42}O_3$ requires C, 78·2; H, 10·2%), $\nu_{max.}$ (in Nujol) 3400 (hydroxyl), 983, 920, 898, and 865 cm.$^{-1}$ (22a-spirostan).

The acetonitrile mother-liquors from the first crystallisation of the crude decomposition product were evaporated to dryness and the residue crystallised from methanol. The solid (1·2 g.) which separated was acetylated with acetic anhydride (20 ml.) and pyridine (20 ml.) on the water-bath for 30 min. The product (0·94 g.), isolated in the usual way, melted at 206—211° after crystallisation from light petroleum (b. p. 60—80°). Its infra-red spectrum was identical with that of 3β-acetoxy-5α : 22a-spirost-11-en (II) (p. 1748) and there was no m. p. depression when samples were mixed.

An alternative method of isolating compound A involved acetylation of the crude reaction product followed by chromatography of the mixed acetates. The product, however, still required repeated crystallisation before it was quite pure and the yield was rather low.

(*b*) Sodium (3 g.) was dissolved in *n*-butanol (800 ml.), the hydrazone (28 g.) was added, and the solution was boiled under reflux for 30 min. The solvent was removed by steam-distillation and the solid which separated was fractionally crystallised from methanol, to give compound A (free alcohol) (9·18 g., 51%), m. p. 110—125°, and 5α : 22a-spirost-11-en-3β-ol (II; 3-HO in place of 3-AcO) (2·1 g., 12%), which crystallised from methanol–methylene chloride in tablets, m. p. 192—194°, $[\alpha]_D$ −37°. [The acetate (II), prepared in the usual way, crystallised from light petroleum in prisms, m. p. 204—208°, $[\alpha]_D$ −43°.]

The solid obtained from the combined mother-liquors from the methanol crystallisations was acetylated and crystallised from light petroleum, to yield 3β-acetoxy-5α : 22a-spirost-11-en (II) [2·6 g.; total yield of (II), 25%], m. p. 204—206°. The mother-liquors from this crystallisation yielded a solid which was chromatographed on alumina (150 g.), giving (V; R = Ac) (700 mg., 3·5%), m. p. 215°, $[\alpha]_D$ −81°. Hirschmann *et al.* (*loc. cit.*) give m. p. 221—225°, $[\alpha]_D$ −80·6° in $CHCl_3$.

Reaction of Compound A with Bromine.—Compound A (0·912 g.) in carbon tetrachloride (40 ml.) was cooled to −25° and treated with bromine (320 mg.) in carbon tetrachloride (2 ml.). The bromine colour was discharged within about 1 min. and a little hydrogen bromide was evolved. The solution was allowed to come to 0°, and was then washed successively with water, aqueous sodium hydrogen carbonate, and water, and dried (Na_2SO_4). Removal of the solvent under reduced pressure left a gum which crystallised on trituration with methanol. The *dibromide* (0·81 g., 66%) was filtered off, washed with a little methanol, and dried. It melted at 108° (decomp.) and had $[\alpha]_D$ −33° (Found: Br, 25·1. $C_{29}H_{44}O_4Br_2$ requires Br, 25·9%), $\nu_{max.}$ (in CS_2) 1735 and 1240 (acetate), 988, 918, 898 and 860 (22a-spirostan) and 702 cm.$^{-1}$ (bromide) (C.S. no. 113). The compound decomposed when kept at room temperature or on attempted crystallisation.

3β : 26-*Diacetoxy*-5α : 22a-*furostan* (III).—Tigogenin acetate (0·5 g.) in acetic acid (25 ml.) was hydrogenated in the presence of Adams catalyst (200 mg.) at room temperature and pressure. After about 24 hr., 1 mol. of hydrogen had been taken up; the catalyst was then filtered off, and the filtrate evaporated to dryness under reduced pressure. The residue was acetylated on the steam-bath for 30 min. with acetic anhydride (10 ml.) and pyridine (10 ml.). The solvents were removed under reduced pressure and the residue crystallised from methanol, to give unchanged tigogenin acetate as needles (0·11 g.), m. p. 204—207°, $[\alpha]_D$ −72°. Dilution of the mother-liquors with water yielded the furostan, which crystallised from aqueous methanol as fine needles (0·2 g.), m. p. 114—116°, $[\alpha]_D$ −14°, $\nu_{max.}$ (in CS_2) .1732 and 1240 cm.$^{-1}$ (acetate). The bands characteristic of the 22a-spirostan system were almost absent. Doukas and Fontaine (*J. Amer. Chem. Soc.*, 1951, **73**, 5917) give m. p. 116—117° and $[\alpha]_D$ −15° in $CHCl_3$.

The free diol, prepared from the diacetate by hydrolysis with ethanolic potassium hydroxide, crystallised in needles, m. p. 165—167°, $[\alpha]_D$ −6°, $\nu_{max.}$ (in Nujol) 3300 cm.$^{-1}$ (hydroxyl). The spirostan bands were absent. Doukas and Fontaine (*loc. cit.*) give m. p. 163—166°, $[\alpha]_D$ −4° in $CHCl_3$.

Epoxidation of Compound A.—Compound A (5 g.) in chloroform (200 ml.) was treated at room temperature with ethereal monoperphthalic acid (2·8N; 15 ml.). After being left for 30 min. at room temperature, the mixture was washed three times with saturated aqueous sodium hydrogen carbonate, then with water, and was dried (Na_2SO_4). The solvent was removed and the residue, which rapidly crystallised, was chromatographed on alumina (Peter

Spence, Type H; 150 g.). Light petroleum–benzene (2 : 1) eluted epoxide P, and benzene and benzene–ether eluted epoxide Q. *Epoxide P* (1·06 g., 21%) melted at 189—190° after crystallisation from aqueous methanol and had $[\alpha]_D$ −66° (Found: C, 73·6; H, 9·3. $C_{29}H_{44}O_5$ requires C, 73·7; H, 9·4%), $\nu_{max.}$ (in CS_2) 1732 and 1240 (acetate), 980, 918, 895, and 860 cm.$^{-1}$ (22a-spirostan).

Epoxide Q (2·01 g., 39%) crystallised from aqueous methanol as colourless needles, m. p. 194—195°, $[\alpha]_D$ −63° (Found: C, 73·9; H, 9·4. $C_{29}H_{44}O_5$ requires C, 73·7; H, 9·4%), $\nu_{max.}$ (in CS_2) 1734 and 1240 (acetate), 980, 918, 895 and 860 (22a-spirostan). A mixture of the two epoxides melted between 140° and 160°. Their infra-red spectra were quite different in detail.

Reduction of Epoxide P.—Epoxide P (0·500 g.) in tetrahydrofuran (50 ml.) was boiled under reflux for 3·5 hr. with lithium aluminium hydride (0·5 g.). After decomposition of excess of hydride, the solution was poured into 0·5N-sulphuric acid (500 ml.) and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to dryness. The residual crystalline solid was heated on the water-bath for 30 min. with acetic anhydride (5 ml.) and pyridine (5 ml.). The solution was poured into water and extracted with ether, and the extract was washed successively with 0·5N-hydrochloric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated to dryness. The crystalline residue (0·487 g.), on recrystallisation from methanol, deposited two forms of crystals, very large prisms, and feathery needles, which were easily separated mechanically. The prisms (0·383 g., 76%), consisting of *diol monoacetate*, melted at 192—194° and had $[\alpha]_D$ −63° (Found: C, 73·3; H, 9·5. $C_{29}H_{46}O_5$ requires C, 73·4; H, 9·8%). $\nu_{max.}$ (in CS_2) 3620 (hydroxyl), 1732 and 1240 (acetate), 978, 918, 898 and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 123). The needles (41 mg.) melted at 185—188°, undepressed on admixture with the starting epoxide.

Dehydration of Alcohol derived from Epoxide P.—The diol monoacetate described in the last paragraph (100 mg.) was treated in pyridine (2 ml.) with phosphorus oxychloride (0·5 ml.). After being left at room temperature for 2 hr., the mixture was poured on crushed ice, and the precipitated solid was filtered off, washed with water, and dried. Crystallisation from methanol gave material (51 mg.), m. p. 138°, undepressed on admixture with compound A. The infra-red spectra of the two samples were identical.

Reduction of Epoxide Q.—Epoxide Q (0·5 g.) in tetrahydrofuran (50 ml.) was reduced with lithium aluminium hydride (0·65 g.) for 5 hr. as described above for the isomer. The product was acetylated and worked up as above, giving, after crystallisation, first from methanol, then from light petroleum, the *diol monoacetate* as prisms (0·306 g., 61%), which melted at 161°, resolidified in needles, and melted finally at 170—171°; $[\alpha]_D$ −53° (*c*, 1·4 in $COMe_2$) (Found: C, 73·5; H, 9·75. $C_{29}H_{46}O_5$ requires C, 73·4; H, 9·8%), $\nu_{max.}$ (in CS_2) 3600 (hydroxyl), 1735 and 1240 (acetate), 980, 916, 897 and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 114).

Dehydration of Alcohol derived from Epoxide Q.—The foregoing diol monoacetate (0·155 g.) in pyridine (2 ml.) was treated with phosphorus oxychloride (0·5 ml.). After being left for 2 hr. at room temperature, the mixture was worked up in the usual way. Crystallisation of the gummy product from methanol gave compound A (0·092 g.), m. p. and mixed m. p. 138—143°.

Oxidation of Compound A with Osmium Tetroxide.—Compound A (1·6 g.) in dry ether (20 ml.) containing pyridine (0·7 ml.) was treated with osmium tetroxide (1·0 g.). The mixture, which began to deposit solid within a few minutes, was left at room temperature for *ca.* 65 hr. Ether was then removed under reduced pressure and the residue boiled under reflux with a solution of sodium sulphite (7·0 g.) in a mixture of ethanol (80 ml.) and water (40 ml.). After 4·5 hr., the solution was cooled and filtered and the residue extracted with boiling ethanol. The combined alcoholic solutions were evaporated to dryness under reduced pressure, the white gummy residue was dissolved in chloroform, and the extract was washed with water, dried (Na_2SO_4), and evaporated to dryness under reduced pressure. This residue was acetylated overnight in acetic anhydride (70 ml.)–pyridine (70 ml.), finally being warmed on the steam-bath for 30 min. The mixture was evaporated to dryness under reduced pressure and the solid residue treated twice with methanol and distilled. The residual gum (1·65 g.) was crystallised from benzene–light petroleum (b. p. 60—80°), giving the triol monoacetate as rosettes of needles (1·18 g., 69%), m. p. 214—217°, $[\alpha]_D$ −40° (Found: C, 70·8; H, 9·4; Ac, 8·6. Calc. for $C_{29}H_{46}O_6$: C, 71·0; H, 9·45; Ac, 8·8%), $\nu_{max.}$ (in CS_2) 3620 (hydroxyl), 1732 and 1240 (acetate), 978, 918, 896, and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 115). Hiskey *et al.* (*loc. cit.*) give m. p. 215—218°, $[\alpha]_D$ −39·3° in $CHCl_3$.

The free *triol* was obtained by hydrolysis of the acetate with methanolic potassium hydroxide on the water-bath for 2 hr. The product crystallised from aqueous methanol in prisms, m. p. 229—233°, $[\alpha]_D$ −40° (Found: C, 72·1; H, 9·8. $C_{27}H_{44}O_5$ requires C, 72·3; H, 9·9%), $\nu_{max.}$ (in CS_2) 3350 (hydroxyl), 982, 918, 900, and 860 cm.$^{-1}$ (22a-spirostan).

Cleavage of the Triol with Periodic Acid.—The above triol (0·46 g.) in methanol (dried, and freshly distilled from 2 : 4-dinitrophenylhydrazine; 25 ml.) was treated with aqueous periodic acid (10%; 5 ml.). The mixture was left for 2 days at room temperature, water was added, and the flocculent precipitate was collected and crystallised from aqueous methanol. The *diketone* separated in needles (0·28 g., 61%), m. p. 157—160°, $[\alpha]_D$ −21° (Found: C, 72·7; H, 9·3. $C_{27}H_{42}O_5$ requires C, 72·6; H, 9·5%), $\nu_{max.}$ (in CS_2) 3620 (hydroxyl), 1740 and 1714 cm.$^{-1}$ (ketones). The band at 1740 cm.$^{-1}$, in the absence of one at *ca.* 1240 cm.$^{-1}$, is attributable to a strained ketone, *e.g.*, a ketone group in a 5-membered ring; the band at 1714 cm.$^{-1}$ is in the normal position for an unstrained ketone, as in an open-chain or 6-membered ring ketone. The compound gave a violet colour with sodium nitroprusside, showing the presence of a methyl ketone grouping, and gave some turbidity on being boiled with Fehling's solution.

Preparation and Methanolysis of 3β-Acetoxy-12β-methanesulphonyloxy-5α : 22a-spirostan (IV; R = Ac).—A solution of hecogenin acetate (10 g.) in ethanol (200 ml.) and methylene chloride (100 ml.) was treated with sodium borohydride (0·6 g.) in water (5 ml.). The mixture was kept for 3 days at room temperature and was then acidified, diluted with methylene chloride, and washed with water. The solvent was evaporated and the residue was crystallised repeatedly from methanol. The 3β-acetoxy-5α : 22a-spirostan-12β-ol (4·2 g., 42%), which melted at 211—216°, was contaminated with the 12α-hydroxy-compound (see below) (Found: C, 73·6; H, 9·7. Calc. for $C_{29}H_{46}O_5$: C, 73·4; H, 9·8%). Mueller, Norton, Stobaugh, Tsai, and Winniford (*J. Amer. Chem. Soc.*, 1953, **75**, 4892) give m. p. 218—220°.

The mixture (4 g.) was added to methanesulphonyl chloride (3 ml.) in pyridine (13 ml.) at 0°. After being left overnight at room temperature, the mixture was poured on ice and ether, and the organic layer was separated, washed successively with dilute hydrochloric acid and sodium carbonate solution, and dried. The residue left on evaporation was boiled under reflux for 2 hr. with methanol (100 ml.). The solution was evaporated to dryness and the residue was hydrolysed with a boiling 4% solution of potassium hydroxide in 80% ethanol for 30 min. The product, isolated with ether, was crystallised twice from methanol to yield compound A (free alcohol) (1·03 g.), m. p. 112 , $[\alpha]_D$ −52°. The acetate, prepared in the usual way, melted at 144—146° and had $[\alpha]_D$ −54°. The identity of this material with that prepared as described above was demonstrated by means of infra-red analysis and mixed m. p. determinations.

The mother-liquors from the crystallisation of compound A (free alcohol) were combined and evaporated and the residue was re-acetylated. The crude acetate was chromatographed on alumina (Peter Spence Grade H; 90 g.). Benzene eluted a further quantity of compound A (800 mg.), m. p. 144—146°, while benzene–chloroform eluted *3β-acetoxy-12α-methanesulphonyloxy-5α : 22a-spirostan* (1·26 g.) which, after crystallisation from methanol, had m. p. 186—188°, $[\alpha]_D$ −21° (Found: C, 65·2; H, 8·7. $C_{30}H_{48}O_7S$ requires C, 65·2; H, 8·7%).

The mother-liquors from the crystallisations of the products from the chromatogram were combined and evaporated. Chromatography of the residue on alumina gave (V; R = Ac) (75 mg.), m. p. 215—216°, $[\alpha]_D$ −80° (Found: C, 75·9; H, 9·8. Calc. for $C_{29}H_{44}O_4$: C, 76·3; H, 9·7%).

Reduction of Hecogenin Acetate with Lithium Aluminium Hydride.—A suspension of hecogenin acetate (5·0 g.) in tetrahydrofuran (25 ml.) was added to lithium aluminium hydride (0·8 g.) in tetrahydrofuran (25 ml.), and the mixture was boiled under reflux for 1 hr. The solution was cooled, excess of hydride was decomposed by addition of ethyl acetate (15 ml.), and the mixture was poured on ice and 2N-sulphuric acid. The product was extracted into chloroform and the extract was dried and evaporated. The residue was treated on the water-bath for 1 hr. with acetic anhydride and pyridine. The solution was evaporated to dryness *in vacuo*, the residue triturated with methanol, and the solvent again evaporated under reduced pressure. The residue (5·31 g.) had $[\alpha]_D$ −52·7°.

The crude product was chromatographed on alumina (Peter Spence Grade H, acid-washed; Brockmann II—III; 150 g.). Benzene–light petroleum (1 : 4) eluted (*a*) crude 12α-acetoxy-compound, m. p. 80—135° (2·12 g.), and (*b*) crude 12β-acetoxy-compound, m. p. 164—176° (1·16 g.). The latter (1·76 g.), in much purer form (m. p. *ca.* 190°), was eluted completely by solvent mixtures ranging from benzene–light petroleum (1 : 2) through benzene to ether–benzene (1 : 9).

Fraction (*a*) from the first column was again chromatographed on alumina (150 g.). Benzene–light petroleum (1 : 4 and 1 : 2) eluted the 12α-acetoxy-compound (0·562 g.), m. p. 145—151°. Further elution with benzene–light petroleum gave a mixed fraction; benzene and ether–benzene (1 : 9) eluted the 12β-acetoxy-compound (0·700 g.), m. p. *ca.* 195°.

3β : 12α-Diacetoxy-5α : 22a-spirostan (XII; R = Ac) (yield 10%) crystallised from aqueous

methanol in prisms, m. p. 153—156°, $[\alpha]_D$ −17° (*c*, 1 in $CHCl_3$), −15° (in $COMe_2$), $\nu_{max.}$ (in CS_2) 1738 and 1240 (acetate), 976, 918, 895, and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 124). Hirschmann *et al.* (*loc. cit.*) give m. p. 156—159°, $[\alpha]_D$ −15° in acetone.

The free diol (XII; R = H), obtained by hydrolysis of the diacetate with ethanolic potassium hydroxide, melted at 200—206° and had $[\alpha]_D$ −30° (in acetone), $\nu_{max.}$ (in Nujol) 3600 and 3450 (hydroxyl) and 981, 919, 903 and 863 cm.$^{-1}$ (22a-spirostan). Hirschmann *et al.* (*loc. cit.*) give m. p. 216—220°, $[\alpha]_D$ −32·4° in acetone.

3β : 12β-Diacetoxy-5α : 22a-spirostan (rockogenin diacetate) (XIII; R = Ac) (yield 45%) melted at 198—203° after crystallisation from methanol, and had $[\alpha]_D$ −68° (*c*, 1 in $CHCl_3$), −63° (in acetone), $\nu_{max.}$ (in CS_2) 1735 and 1240 (acetate), 978, 918, 898, and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 116). Hirschmann *et al.*, *loc. cit.*) give m. p. 202—206·5°, $[\alpha]_D$ −65·1° in acetone.

The free diol (XIII; R = H) melted at 216—219° and had $[\alpha]_D$ −60° (in acetone), $\nu_{max.}$ (in Nujol) 3300 (hydroxyl) and 973, 914, 892, and 860 cm.$^{-1}$ (22a-spirostan). Hirschmann *et al.* (*loc. cit.*) give m. p. 218·5—220·5°, $[\alpha]_D$ —63·8° in acetone.

12α-*Acetoxy*-5α : 22a-*spirostan*-3β-*ol* (XIV).—3β : 12α-Diacetoxy-5α : 22a-spirostan (0·750 g.) was boiled under reflux for 2 hr. with potassium hydrogen carbonate (0·225 g.) in methanol (24 ml.) and water (6 ml.). The crystalline solid (585 mg., 85%) which had separated was collected by filtration and used as such in the next stage. A portion, crystallised twice from ethanol, gave the *diol monoacetate* with m. p. 231—233° and $[\alpha]_D$ −15° (Found: C, 73·4; H, 9·5. $C_{29}H_{46}O_5$ requires C, 73·4; H, 9·8%), $\nu_{max.}$ (in CS_2) 3620 (hydroxyl), 1739 and 1240 (acetate), 978, 920, 898, and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 117).

12α-*Acetoxy*-5α : 22a-*spirostan*-3-*one* (XV; R = Ac).—The foregoing monoacetate (0·55 g.) in glacial acetic acid (15 ml.) was treated with chromic anhydride (1·5 equiv.) and left at room temperature for 4 hr. Excess of chromic anhydride was destroyed with methanol, some of the solvent was removed, and the residue was diluted with water. The *ketone* (0·50 g., 91%), crystallised from aqueous ethanol, had m. p. 214—217°, $[\alpha]_D$ +1° (Found: C, 73·6; H, 9·4. $C_{29}H_{44}O_5$ requires C, 73·7; H, 9·4%), $\nu_{max.}$ (in CS_2) 1739 and 1237 (acetate), 1715 (ketone), 981, 920, 899, and 863 cm.$^{-1}$ (22a-spirostan) (C.S. no. 118).

The free *alcohol* (XV; R = H), obtained from the acetate with methanolic potassium hydroxide, melted at 254—257° after crystallisation from aqueous alcohol and had $[\alpha]_D$ −30° (Found: C, 75·6; H, 9·8. $C_{27}H_{42}O_4$ requires C, 75·3; H, 9·8%), $\nu_{max.}$ (in CS_2) 3620 (hydroxyl), 1712 (ketone), 979, 917, and 895 cm.$^{-1}$ (22a-spirostan).

Oxidation of Compound A (Free Alcohol) with Chromic Anhydride.—The alcohol (1·0 g.) in glacial acetic acid (15 ml.) was treated with chromic anhydride in acetic acid (0·55N; 17 ml.), and the mixture was left at room temperature for 4 hr. Excess of chromic anhydride was destroyed with methanol, and the product was worked up in the usual way. The *ketone* melted at 101—104° and had $[\alpha]_D$ —40° (Found: C, 78·3; H, 9·8. $C_{27}H_{40}O_3$ requires C, 78·6; H, 9·8%), $\nu_{max.}$ (in CS_2) 1715 (ketone), 980, 920, 900, and 860 cm.$^{-1}$ (22a-spirostan). The 2 : 4-*dinitrophenylhydrazone* was an orange compound, m. p. 206—208° (Found: N, 9·8. $C_{33}H_{44}O_6N_4$ requires N, 9·5%).

3β-*Acetoxy*-5α : 22a-*spirost*-11-*en* (II).—3β-Acetoxy-12α : 23-dibromo-5α : 22a-spirostan-11β-ol (Cornforth and Osbond, *loc. cit.*) (3·0 g.) was boiled under reflux for 3·5 hr. with stirring with zinc dust (acid-washed; 30 g.) and glacial acetic acid (300 ml.). The hot solution was filtered, the solid washed with hot acetic acid, and the combined filtrate and washings were evaporated to small bulk and diluted with water. The *product* (2·05 g.; m. p. 187—200°) was crystallised from acetone, to give prisms (1·41 g.), m. p. 202—205° and a second crop (0·27 g.) with slightly lower m. p. (total yield 78%). Further crystallisation from acetone raised the m. p. to 206—210°; $[\alpha]_D$ was −44° (Found: C, 76·3; H, 9·65. $C_{29}H_{44}O_4$ requires C, 76·3; H, 9·7%). $\nu_{max.}$ (in CS_2) were 1732 and 1240 (acetate), 978, 918, 895, and 860 cm.$^{-1}$ (22a-spirostan). Strong maxima at 703 and 760 cm.$^{-1}$ suggest the presence of a *cis*-1 : 2-disubstituted ethylene grouping; this is supported by a shoulder (at 3000 cm.$^{-1}$) on the strong C–H stretching band at 2950 cm.$^{-1}$ (cf. Sheppard and Simpson, *Quart. Reviews*, 1952, **6**, 1) (C.S. no. 119).

The same Δ^{11}-compound was obtained by a similar method from 3β-acetoxy-23-bromo-11β : 12β-epoxy-5α : 22a-spirostan (Cornforth and Osbond, *loc. cit.*). The yield in this case was only about 30%.

The free *alcohol*, obtained by hydrolysis of the acetate with ethanolic sodium hydroxide, was a solvate, m. p. 184—188° after crystallisation from methanol. After being dried at 120°/0·1 mm., it melted at 193—195° and had $[\alpha]_D$ −36° (Found: C, 77·8; H, 10·2. $C_{27}H_{42}O_3$ requires C, 78·2; H, 10·2%), $\nu_{max.}$ (in Nujol) 3560 and 3330 (hydroxyl), 978, 918, 900, and 861 cm.$^{-1}$ (22a-spirostan). This compound, like the acetate, showed bands of medium intensity at 702 and

760 cm.$^{-1}$ and a shoulder at 3000 cm.$^{-1}$, indicative of the presence of a *cis*-1 : 2-disubstituted ethylene grouping.

3β-*Acetoxy*-11α : 12α-*epoxy*-5α : 22a-*spirostan* (XX).—3β-Acetoxy-5α : 22a-spirost-11-en (200 mg.) in chloroform (6 ml.) was treated with ethereal monoperphthalic acid (2·8N; 0·5 ml.). After being left overnight in the refrigerator, the solution was washed consecutively with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated to dryness. The residual white solid was crystallised from aqueous acetone, to yield the *epoxide* as needles (155 mg., 75%), m. p. 221—225°, $[\alpha]_D$ −49·5° (Found: C, 73·4; H, 9·3. $C_{29}H_{44}O_5$ requires C, 73·7; H, 9·4%), $\nu_{max.}$ (in CS_2) 1735 and 1240 cm.$^{-1}$ (acetate), 978, 918, 895, and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 120). There was no indication of the presence of the isomeric 11β : 12β-epoxide.

5α : 22a-*Spirostan*-3β : 12α-*diol* (XII; R = H).—The foregoing epoxide (0·5 g.) was boiled under reflux for 2 hr. with a solution of lithium aluminium hydride (0·6 g.) in tetrahydrofuran (25 ml.). The excess of hydride was destroyed and the product isolated in the usual way. Crystallisation of the crude diol (0·5 g.) from methanol gave material with m. p. 207—214°, $[\alpha]_D$ −30° (*c*, 1·05 in $COMe_2$). The m. p. of a mixture of this material and a sample of (XII; R = H) prepared as described on p. 1748 was not depressed; the infra-red spectra of the specimens were identical.

The diacetate (XII; R = Ac), obtained from the crude diol with pyridine–acetic anhydride on the water-bath, melted at 153—155° after crystallisation from aqueous methanol and had $[\alpha]_D$ −14° (*c*, 1·0 in $COMe_2$). The m. p. of a mixture of this material with an authentic sample was undepressed and the infra-red spectra were identical. The diacetate was obtained in 44% yield from epoxide.

Hecogenone (XXI).—The crude 3β : 12α-diol prepared as described above (200 mg.) in acetic acid (7 ml.) was treated with 0·55N-solution of chromic anhydride in acetic acid (5·5 ml.). The solution was left at room temperature for 4 hr., excess of chromic anhydride was destroyed with methanol, and the product poured into water. Crystallisation from methanol gave hecogenone as plates, m. p. 232—235°, $[\alpha]_D$ +21°, $\nu_{max.}$ (in CS_2) 1710 (ketone), 978, 918, 896 and 860 cm.$^{-1}$ (22a-spirostan) (C.S. no. 121). The material was identical with a sample prepared from rockogenin by the same method. Marker, Wagner, Ulshafer, Wittbecker, Goldsmith, and Ruof (*J. Amer. Chem. Soc.*, 1947, **69**, 2167) give m. p. 237—240°.

Solvolysis of 3β-*Acetoxy*-12β-*methanesulphonyloxy*-5α : 22a-*spirostan in Presence of Base. Compound* (V).—Rockogenin 3-monoacetate was prepared as described above, and was chromatographed on acid-washed alumina (Brockmann II—III). The material eluted with benzene was crystallised from methanol and then had m. p. 214—219°, $[\alpha]_D$ −65° (in $CHCl_3$), −61° (in dioxan), $\nu_{max.}$ 3620 (hydroxyl), 1736 and 1238 (acetate), 978, 918, 895, and 862 (22a-spirostan) in CS_2 (C.S. no. 122). Mueller, Norton, Stobaugh, Tsai, and Winniford (*J. Amer. Chem. Soc.*, 1953, **75**, 4892) give m. p. 218—220°, $[\alpha]_D$ −58° in dioxan.

This material (4·4 g.) was treated with methanesulphonyl chloride as described above. The residue left after evaporation of the ethereal solution was a solid, m. p. 125—130° (decomp.). This material was boiled under reflux for 4 hr. with a solution made by dissolving potassium (1·5 g.) in *tert.*-butanol (100 ml.). The solution was poured into water, and the product isolated with ether. Crystallisation from acetonitrile gave the *product* (V; R = H) (2·8 g., 73%), m. p. 157—169°, $[\alpha]_D$ −66·5° (Found: C, 78·3; H, 10·1. $C_{27}H_{42}O_3$ requires C, 78·2; H, 10·2%), $\nu_{max.}$ 1642 and 886 (1 : 1-disubstituted ethylene), 980, 920, 898, and 864 cm.$^{-1}$ (22a-spirostan) in CS_2. The presence of hydroxyl was shown by the spectrum of a Nujol mull, which had maxima at 3500 and 3280 cm.$^{-1}$.

The acetate (V; R = Ac) melted at 218—223° and had $[\alpha]_D$ −78·2°, $\nu_{max.}$ 1732 and 1238 (acetate), 1638 and 884 (1 : 1-disubstituted ethylene), 978, 918, 896, and 862 cm.$^{-1}$ (22a-spirostan) in CS_2.

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