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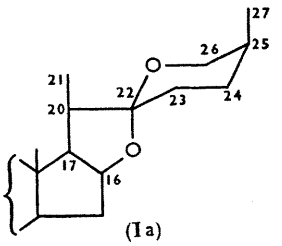
903. *The Stereochemistry of the Side-chain of the Steroidal Sapogenins : Configuration at* $C_{(22)}$ *of Normal and* iso-*Sapogenins.*

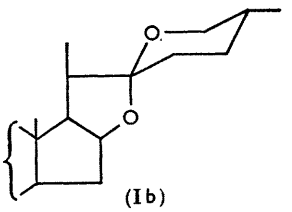
By R. K. Callow and (Miss) P. N. Massy-Beresford.

3β-Acetoxy-5α-25*L*- and -25*D*-spirostan-23-one * have been prepared, and both have been converted, *via* the 24-bromo-derivatives, into 3β : 24-diacetoxy-5α-spirost-24-en-23-one. This provides chemical evidence that the normal and *iso*-sapogenins differ only in configuration at $C_{(25)}$. The absolute configuration of these compounds at $C_{(22)}$ is discussed.

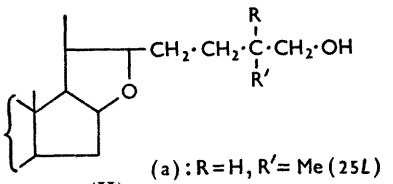
The natural steroid sapogenins occur in two isomeric series, the "normal" and "*iso*"-sapogenins, which differ in steric orientation in the side-chain, the former being converted into the latter by hydrogen chloride under certain conditions. Marker and Rohrmann [1] suggested that this isomerisation consists of a change of configuration at $C_{(22)}$ involving the opening and reclosure of ring F. Scheer, Kostic, and Mosettig [2] showed that the two series differ in configuration at $C_{(25)}$, and James [3] related the configuration at this asymmetric centre to glyceraldehyde, so that the "normal" and "*iso*"-series may be referred to as 25*L* (Ia) and 25*D* (Ib) respectively.



(Ia)



(Ib)



(II)

(a) : R = H, R′ = Me (25*L*)

(b) : R = Me, R′ = H (25*D*)

There remained the possibility that the two series differ in configuration at $C_{(22)}$ as well as at $C_{(25)}$. Scheer, Kostic, and Mosettig [4] later showed that dihydrosarsapogenin (IIa) and dihydrosmilagenin (IIb) differ only at $C_{(25)}$, but the possibility that inversion at $C_{(22)}$ had occurred during the opening of ring F could not be excluded. It has also been shown [5] that inversion at $C_{(25)}$ occurs without the opening of ring F, but as this is an unusual reaction further chemical evidence that the two series have the same configuration at $C_{(22)}$ was

* In this extension of the general convention, the capital italic *D* in 25*D* denotes that $C_{(27)}$ lies to the right when in a Fischer projection formula $C_{(24)}$ is written above, and $C_{(26)}$ is written below, $C_{(25)}$. 25*L* denotes that in a similar projection formula $C_{(27)}$ lies to the left.—Ed.

[1] Marker and Rohrmann, *J. Amer. Chem. Soc.*, 1939, **61**, 846.
[2] Scheer, Kostic, and Mosettig, *ibid.*, 1953, **75**, 4871.
[3] James, *J.*, 1955, 637.
[4] Scheer, Kostic, and Mosettig, *J. Amer. Chem. Soc.*, 1955, **77**, 641.
[5] Callow and James, *J.*, 1955, 1671.

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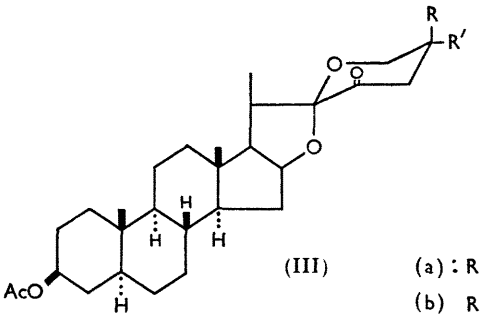
desirable. This could be obtained if two sapogenins, diastereoisomeric at position 25, could be converted, by reactions involving conditions under which isomerisation at $C_{(22)}$ is unlikely, into compounds in which the asymmetry at $C_{(25)}$ has been destroyed by introduction of a double bond between $C_{(25)}$ and an adjacent carbon atom. This has now been achieved: the identity of the unsaturated compounds obtained from *neo*tigogenin (25*L*) and tigogenin (25*D*) shows that there is only a single difference between these sapogenins, namely, the configuration at $C_{(25)}$.

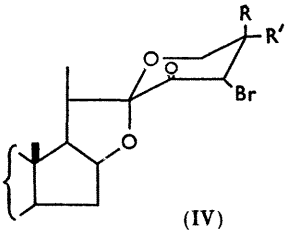
Controlled oxidation of sarsasapogenin acetate by chromic acid yields a sapogenin, containing a ketone group in ring F, which Marker and Shabica [6] suggested was 23-oxo-sarsasapogenin acetate. This reaction seemed to offer a convenient entry into ring F, and its application to *neo*tigogenin and tigogenin acetates was investigated. These sapogenins yielded the previously undescribed 23-oxo-derivatives (IIIa and b), obtained pure by means of the special method of separation by use of reagent T, recommended by Girard and Sandulesco [7] for ketones of high molecular weight, in yields of 8·8% and 2·4%, respectively. The usual Girard procedure resulted in the formation of inseparable emulsions. The 23-oxo-compounds have an infrared band at 1727 cm.$^{-1}$, and show marked differences from the parent sapogenins in the "fingerprint" region. There is weak ultraviolet absorption at about 300 mμ (log ε 1·5). The ketones form crystalline semicarbazones. In the 25*D*-series the formation of the semicarbazone from the ketone is accompanied by a large increase in dextrorotation ($\Delta[M]_D$ +171°) whereas in the 25*L*-series there is a small change in the opposite direction ($\Delta[M]_D$ −44°). Huang-Minlon reduction of (IIIa and b) yields the parent sapogenins, showing that no configurational changes occurred during the oxidation by chromic acid.



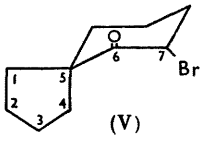
(III)

(a): R = Me, R′ = H (25*L*)

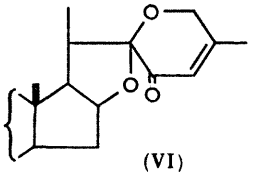
(b) R = H, R′ = Me (25*D*)



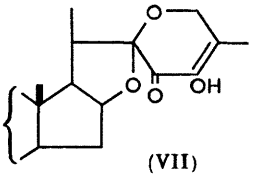
(IV)



(V)



(VI)



(VII)

Crystalline 24-bromo-23-oxosapogenin acetates (IVa and b) were obtained in 30—40% yield by bromination in chloroform–acetic acid. Bromination caused a displacement of the infrared carbonyl absorption to a higher frequency (1745 cm.$^{-1}$) in both the 25*L*- and the 25*D*-compound, and the weak ultraviolet absorption is at 296 mμ (log ε 1·8). This is evidence [8,9] that the bromine has entered the equatorial position in both compounds. Although the preferred conformation for the C–Br bond in 2-bromo*cyclo*hexanones is axial,[10] steric repulsion between an axial bromine and other substituents suffices in some

[6] Marker and Shabica, *J. Amer. Chem. Soc.*, 1942, **64**, 813.
[7] Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1095.
[8] Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[9] Cookson, *J.*, 1954, 282.
[10] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 2301.

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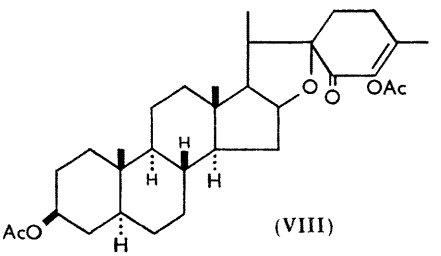
cases to overcome the electrostatic repulsion of the C–Br (equatorial) and C=O dipoles, with the result that the more stable conformation is that in which the bromine is equatorial. This is known to occur [10] in 7-bromo*spiro*[4 : 5]decan-6-one (V) which exists predominantly as the equatorial isomer. There would be considerable 1 : 3-interaction between an axial bromine atom and the 4-methylene group of the *cyclo*pentane ring. The 24-bromo-23-oxosapogenins (IVa and b) are structurally analogous, so there would be steric repulsion between an axial bromine atom at position 24 and the oxygen atom of ring E. The carbon–bromine absorptions appear at 670 and 697 cm.$^{-1}$, respectively, in CS_2 solution. The compounds (IVa and b) were debrominated by zinc dust in alcohol to give the parent ketones in good yield, so that no changes in the configuration of the side-chain had occurred during bromination.

Dehydrobromination of compounds (IVa and b) by boiling collidine gave very low yields of the αβ-unsaturated ketone (VI), especially from the latter, presumably owing to the *cis*-relation of the bromine and the hydrogen atom at $C_{(25)}$. This approach was abandoned when another route to 24 : 25-unsaturated derivatives proved successful.

Hydrolysis of compounds (IVa and b) by ethanolic potassium hydroxide at room temperature proceeded with simultaneous autoxidation of the α-ketols, to give, in both series, 3β : 24-dihydroxy-5α-spirost-24-en-23-one (VII), the enolic form of the 23 : 24-dioxosapogenins. This compound absorbs in the infrared at 1690(m) and 1660(s) cm.$^{-1}$ in $CHCl_3$ solution. It is suggested that the band at 1690 cm.$^{-1}$ is due to the αβ-unsaturated carbonyl group, and the band at 1660 cm.$^{-1}$ is the absorption of the same group when internally hydrogen-bonded. The hydroxyl absorption, consisting of two broad bands at about 3480 and 3100 cm.$^{-1}$ (KCl disc), also indicates strong hydrogen bonding in the solid state. The compound is surprisingly insoluble in methanol for a sapogenin derivative containing two hydroxyl groups. Its ultraviolet absorption is at 276 mμ (log ε 4·0). The autoxidation of the intermediate 24-hydroxy-23-oxosapogenins is analogous to that of benzoin to benzil [11] in alkaline solution in the presence of atmospheric oxygen.



(VIII)

The samples of the enol (VII) derived from *neo*tigogenin and tigogenin were converted into the 3β : 24-diacetate (VIII), and a detailed comparison of the two samples was made. They had identical melting points, optical rotations, infrared absorption spectra in $CHCl_3$ solution and in KCl discs, and ultraviolet absorption spectra, and single crystals of the two samples gave identical *X*-ray diffraction patterns. Thus *neo*tigogenin and tigogenin must differ only in configuration at $C_{(25)}$.

Some other reactions of the 23-oxosapogenins have been studied, but the low yields in which these compounds are obtainable prevented a thorough investigation of the less promising reactions.

Sodium borohydride in methanol reduces the 23-oxo-group, and crystalline 3β : 23-dihydroxy- and 3β-acetoxy-23-hydroxy-derivatives were obtained in both series. (No attempt was made to separate 23*a*- and 23*b*-isomers.) We had hoped that it would be possible to replace the 23-hydroxyl group by halogen, thus correlating the 23-oxosapogenins with the 23-halogenosapogenins obtained by direct halogenation. The results

[11] Weissberger, *Ber.*, 1932, **65**, 1815.

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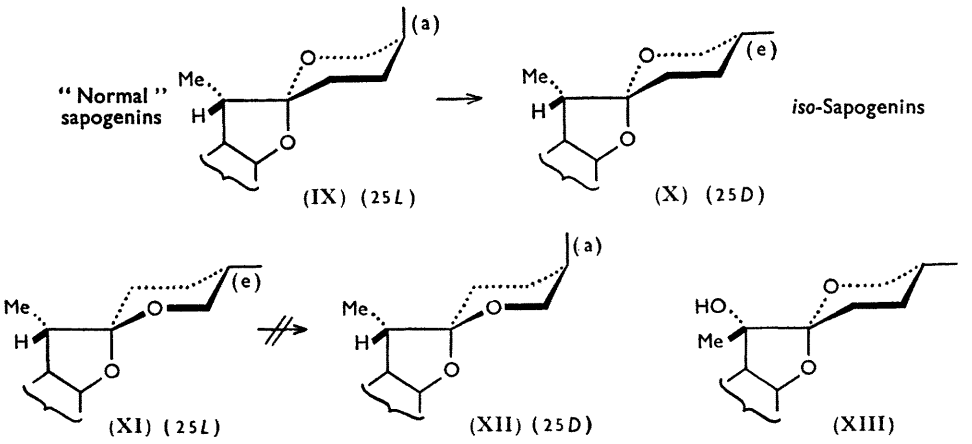
were not encouraging. 3β-Acetoxy-23-hydroxy-5α-25*D*-spirostan with phosphorus pentachloride in carbon tetrachloride containing calcium carbonate in suspension yielded chlorine-containing gums whose infrared absorption did not resemble that of 23-chlorotigogenin acetate prepared by direct chlorination of tigogenin acetate. 3β-Acetoxy-23-hydroxy-5α-25*L*-spirostan was converted into the 23-methanesulphonate, and the gummy product treated with lithium bromide in various solvents: no replacement of the methanesulphonyloxy-group occurred, and there was evidence from infrared absorption that this treatment had destroyed the spiroketal system.

Attempts to prepare a *pseudo*-derivative of the ketone (IIIa) yielded gums which showed no infrared or ultraviolet absorption attributable to an αβ-unsaturated ketone.

Dr. Carl Djerrassi measured the optical rotatory dispersion curves of compounds (IIIa and b), (IVa and b), (VI), and (VIII) over the range 280—700 mμ, and has kindly given us permission to quote the results. The 23-oxosapogenins show similar curves with a positive peak at 330 mμ.[12] Since a change of configuration at $C_{(25)}$ would not be expected to cause an inversion of the curve, this is consistent with the configurational identity of the compounds at $C_{(22)}$. It was hoped that some information as to the absolute configuration about $C_{(22)}$ might be obtained from the curves for the 24-bromo-23-oxosapogenins, since for axial 24-bromo-23-ketones derived from (IX) and (X) the curves should be positive, while those derived from (XI) and (XII) should give negative rotatory dispersion curves irrespective of the orientation of $C_{(27)}$. The curves obtained confirmed the evidence from infrared and ultraviolet absorption spectra that the compounds are equatorial α-bromo-ketones, so that no conclusions could be drawn from the results.

The discussion of the configuration of the sapogenins at $C_{(22)}$ must take into account the relative stability of the two series as indicated by the conversion of normal into *iso*-sapogenins. It is logical to assume that this change at $C_{(25)}$ is a change from an axial conformation of the methyl group to an equatorial one. Application of the method of conformational analysis led us to conclusions mainly identical with those reached by Hirschmann *et al.*[13] In particular ring F is in a prone position with the 23 : 24-bond parallel to the 20 : 22-bond. The assignment of the α- or β-position to the $C_{(22)}$–O bond in ring F involves some uncertain assumptions of the strength of interactions, and Hirschmann *et al.* felt justified in assigning to this bond the β-position in the normal and the α-position



in the *iso*-sapogenins. Now, however, that it has been shown that the configuration at $C_{(22)}$ is the same in both series, it is clear that, with the absolute configuration at $C_{(25)}$

[12] See Djerassi and Klyne, *Proc. Chem. Soc.*, 1957, 55, for nomenclature.
[13] Hirschmann, Hirschmann, and Corcoran, *J. Org. Chem.*, 1955, **20**, 572.

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known, the conformation of ring F with the methyl group axial is to be assigned to the normal sapogenins (IX), and the conformation with the methyl group equatorial to the *iso*-sapogenins (X), both these conformations having the oxygen atom in the α-position. If the oxygen atom were in the β-position, as in (XI) and (XII), the conformations of the methyl groups would be inconsistent with the known relative stability of the two series.

Wall and Walens * have shown that 20α-hydroxy-20-*iso*tigogenin (XIII) has the same configuration as tigogenin at $C_{(22)}$, and has an infrared absorption in the hydroxyl region indicative of strong hydrogen bonding, to be attributed to bonding between the oxygen atom of ring F and the 20α-hydroxyl group. This is additional evidence in favour of the α-position for the $C_{(22)}$–O bond in the natural sapogenins.

Experimental

M. p.s were determined in a Kofler apparatus with polarised light, and are corrected. Optical rotations were determined in $CHCl_3$ solutions of concentration 1·0% unless otherwise stated. Samples for analysis were recrystallised to constant m. p. and dried at 80°, 100°, or 140° in a high vacuum. Ultraviolet absorption spectra were measured in methanol. Infrared absorption was measured with a double-beam instrument with a rock-salt prism (Perkin-Elmer Model 21) in KCl discs unless otherwise stated.

23-*Oxo*neo*tigogenin Acetate*.—*neo*Tigogenin acetate (10 g.) was oxidised with chromic acid in acetic acid solution at 60° by Fieser and Jacobsen's method.[14] Crystallisation of the neutral fraction from methanol separated the ketone and unchanged *neo*tigogenin acetate from lactone acetate which remained in the mother-liquors. The mixture of ketone and sapogenin acetates (1·6 g.) in ethanol (67·5 ml.) and glacial acetic acid (7·5 ml.), and Girard's reagent T (3·0 g.) were boiled under reflux for 2 hr. Ethylene glycol (67·5 ml.) was added and the ethanol evaporated under reduced pressure from the steam-bath. After cooling, the mixture was extracted six times with dry benzene, and the extracts were washed with glycol, then with water, dried, and evaporated, to give *neo*tigogenin acetate (0·68 g.). The glycol fractions were diluted with water, glacial acetic acid (50 ml.) was added, and the mixture heated at 100° for 3 hr. After cooling, the solid was collected, washed, and dried *in vacuo* over P_2O_5 (0·906 g., 8·8%). This method gives a complete separation of ketonic from non-ketonic material in one operation. Recrystallised from methanol, 23-*oxo*neo*tigogenin acetate* has m. p. 231—234°, $[\alpha]_D$ −49° (Found: C, 73·7; H, 9·4. $C_{29}H_{44}O_5$ requires C, 73·7; H, 9·4%), $\lambda_{max.}$ 302—304 mμ (log ε 1·5), $\nu_{max.}$ 1730 cm.$^{-1}$ (ketone and acetate). Hydrolysis of the acetate by 5% potassium hydroxide solution in boiling ethanol and recrystallisation from acetone–light petroleum (b. p. 60—80°) gave 23-*oxo*neo*tigogenin*, m. p. 244—247°, $[\alpha]_D$ −56° (*c* 0·78%) (Found: C, 75·2; H, 9·6. $C_{27}H_{42}O_4$ requires C, 75·3; H, 9·8%), $\lambda_{max.}$ 300—304 mμ (log ε 1·6), $\nu_{max.}$ 1727 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 1732 cm.$^{-1}$.

The acid fraction from the oxidation gave neo*tigogenoic acid*, m. p. 212—216° (from methanol), $[\alpha]_D$ −153° (*c* 0·2%) (Found: C, 72·5; H, 9·5. $C_{27}H_{42}O_5$ requires C, 72·6; H, 9·5%), $\nu_{max.}$ 1737 ($C_{(16)}$-ketone), 1712 ($C_{(22)}$-ketone), 1680 cm.$^{-1}$ (internally hydrogen-bonded carboxyl group). Treatment with ethanolic 3% sodium hydroxide for 2 hr. under reflux gave *anhydro*neo*tigogenoic acid*, m. p. 238—240° (from chloroform–ether), $[\alpha]_D$ −137° (*c* 0·56%) (Found: C, 75·4; H, 9·4. $C_{27}H_{40}O_4$ requires C, 75·7; H, 9·4%), $\lambda_{max.}$ 244 mμ (log ε 4·2), $\nu_{max.}$ 1715, 1693, 1660(s) cm.$^{-1}$.

23-Oxo*neo*tigogenin acetate (139 mg.) in ethanol (25 ml.) and a solution of semicarbazide hydrochloride (200 mg.) and sodium hydrogen carbonate (100 mg.) in water (1 ml.) were boiled for 7½ hr., then poured into water and extracted with chloroform, and the extract was washed, dried, and evaporated. Crystallised from ethyl acetate, the *semicarbazone* has m. p. 232—240° (decomp.), $[\alpha]_D$ −52° (Found: C, 67·7; H, 8·9; N, 7·8. $C_{30}H_{47}O_5N_3$ requires C, 68·0; H, 8·9; N, 7·9%), $\nu_{max.}$ 3430, 3260—3180, 1730 (acetate), 1700 (amide I, carboxyl), 1670 (C=N), 1580 (amide II), 1250 (acetate), 760 (NH rocking) cm.$^{-1}$.[15]

23-*Oxotigogenin Acetate*.—Tigogenin acetate (10 g.), prepared from hecogenin acetate and freed from traces of the latter by Girard separation, was oxidised as described for *neo*tigogenin

* We are indebted to Dr. Walens for the personal communication of their results before publication (*Chem. and Ind.*, 1957, 818).

[14] Fieser and Jacobsen, *J. Amer. Chem. Soc.*, 1938, **60**, 28.
[15] Davison and Christie, *J.*, 1955, 3389.

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acetate but at 70—90°. Girard separation by the special method described above, yielded 1·83 g. of tigogenin acetate and 0·53 g. of crude 23-oxotigogenin acetate, purified from further traces of hecogenin acetate by crystallisation from methanol (yield of pure ketone 247 mg., 2·4%). 23-*Oxotigogenin acetate* has m. p. 233—235° (from methanol), $[\alpha]_D$ −53° (Found: C, 73·7; H, 9·1%), $\lambda_{max.}$ 298—300 mμ (log ε 1·5), $\nu_{max.}$ 1730 cm.$^{-1}$. Hydrolysis of the acetate gave 23-*oxotigogenin*, m. p. 232—234° (from methanol), $[\alpha]_D$ −43° (Found: C, 75·0; H, 9·7%), $\lambda_{max.}$ 300—302 mμ (log ε 1·5), $\nu_{max.}$ 1722 cm.$^{-1}$, $\nu_{max.}$ (in $CHCl_3$) 1730 cm.$^{-1}$. 23-*Oxotigogenin acetate semicarbazone*, prepared as described for the 25*L*-derivative, has m. p. 212—215° (from ethyl acetate), $[\alpha]_D$ −15° (Found: C, 67·9; H, 9·0; N, 7·8%), $\nu_{max.}$ 3420, 3100, 2960, 1725, 1694, 1575, 1250, 755 cm.$^{-1}$.

Huang-Minlon Reduction of 23-*Oxo*neo*tigogenin Acetate*.—23-Oxo*neo*tigogenin acetate (200 mg.), ethylene glycol (50 ml.), potassium hydroxide (6·5 g.), water (6·5 ml.), and hydrazine hydrate (100%; 5 ml.) were boiled under reflux for 2 hr. The water and excess of hydrazine were then distilled off, and the mixture boiled at 195° for 2 hr. After cooling, it was poured into water, and neutralised, and the solid collected, washed, and dried *in vacuo* over P_2O_5. The product was chromatographed and yielded 168 mg. (95%) of *neo*tigogenin which, after recrystallisation, had the elementary composition, m. p., $[\alpha]_D$, and infrared absorption of authentic material.

Huang-Minlon Reduction of 23-*Oxotigogenin*.—This was carried out as described above. 206 mg. of 23-oxotigogenin yielded 190 mg. (95%) of crude tigogenin which, after recrystallisation, had the elementary composition and physical properties of authentic material.

Bromination of 23-*Oxo*neo*tigogenin Acetate*.—To a solution of 23-oxo*neo*tigogenin acetate (894 mg., 1·89 mmoles) in chloroform (20 ml.) and glacial acetic acid (40 ml.) stirred at 35°, were added 3 drops of concentrated hydrobromic acid and then 3·42 mmoles of bromine (17·5 ml. of a 1% v/v solution of bromine in glacial acetic acid) during 20 min. The solution was stirred at room temperature for 1 hr., poured into water, and extracted with chloroform. The extract was washed with sodium hydrogen carbonate solution until free from acid, then with thiosulphate solution and with water, dried, and evaporated under reduced pressure at room temperature. The black gum was chromatographed on neutral alumina. Benzene–light petroleum (b. p. 60—80°) (2 : 3) eluted the α-bromo-ketone (471 mg., 45%). Crystallisation from methanol gave 24-*bromo*-23-*oxo*neo*tigogenin acetate*, m. p. 190—194° (decomp.), $[\alpha]_D$ −76° (Found: C, 63·1; H, 8·0; Br, 14·3. $C_{29}H_{43}O_5Br$ requires C, 63·2; H, 7·9; Br, 14·5%), $\lambda_{max.}$ 297 mμ (log ε 1·9), $\nu_{max.}$ 1745 (shoulder; C=O), 1728 (acetate), 1260 (acetate), 750, 660 (C–Br) cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 749, 670, 606, 586, 530 cm.$^{-1}$.

Bromination of 23-*Oxotigogenin Acetate*.—23-Oxotigogenin acetate (820 mg.) was brominated at 42° and chromatographed as described above, and yielded 302 mg. (32%) of material which recrystallised from methanol to give 24-*bromo*-23-*oxotigogenin acetate*, m. p. 211—216°, $[\alpha]_D$ −60° (Found: C, 63·4; H, 8·1; Br, 14·7%), $\lambda_{max.}$ 296 mμ (log ε 1·8), $\nu_{max.}$ 1743 (shoulder), 1732, 1250, 695 (C–Br), 657 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 743(w), 697, 662, 614 and 606 (doublet), 579(w), 532 cm.$^{-1}$.

Debrominations.—24-Bromo-23-oxo*neo*tigogenin acetate (75 mg.) in ethanol (50 ml.) was boiled under reflux with stirring for 3 hr. with zinc dust (3 g.). The zinc was filtered off and the filtrate evaporated to give 23-oxo*neo*tigogenin acetate (70 mg.) which, after two recrystallisations, gave analytical figures and had physical properties identical with those of an authentic sample.

Similar debromination of 24-bromo-23-oxotigogenin acetate gave 23-oxotigogenin acetate in high yield, identical with an authentic sample.

Hydrolyses.—A solution of 24-bromo-23-oxo*neo*tigogenin acetate (286 mg.) and potassium hydroxide (3 g.) in water (15 ml.) and ethanol (115 ml.) was stirred at room temperature for 3 hr. Carbon dioxide was then passed into the solution until the pH was about 8, water was added, and the solution extracted with chloroform. The extract was washed with 2N-sodium carbonate and water, dried, and evaporated and the residue (145 mg., 63%) crystallised from methanol to give plates of 3β : 24-*dihydroxy*-5α-*spirost*-24-*en*-23-*one*, m. p. 263—273°, $[\alpha]_D$ −88° (*c* 0·44%) (Found: C, 72·6; H, 9·0. $C_{27}H_{40}O_5$ requires C, 72·9; H, 9·1%), $\lambda_{max.}$ 276 mμ (log ε 4·0), $\nu_{max.}$ 1685(m), 1657(s), $\lambda_{max.}$ (in $CHCl_3$) 1690(m), 1662(s) cm.$^{-1}$. The aqueous layer from the hydrolysis and the carbonate washings were acidified to give an unidentified acid fraction (51 mg.).

24-Bromo-23-oxotigogenin acetate (411 mg.) was hydrolysed as described above, and the product (0·26 g., 78%) recrystallised, to give the same enol, m. p. 263—273°, $[\alpha]_D$ −85° (*c* 0·42%)

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(Found: C, 72·9; H, 9·5%), $\lambda_{max.}$ 275 mμ (log ε 4·0), $\nu_{max.}$ 1685, 1658, $\nu_{max.}$ (in $CHCl_3$) 1695(m), 1664(s) cm.$^{-1}$. The aqueous layers yielded 130 mg. of unidentified acidic material.

3β : 24-*Diacetoxy-5α-spirost-24-en-23-one*.—Samples of 3β : 24-dihydroxy-5α-spirost-24-en-23-one derived from *neo*tigogenin and tigogenin were acetylated in pyridine–acetic anhydride (1 : 1) at room temperature. The solvents were evaporated under reduced pressure from the steam-bath, and the residues dissolved in carbon tetrachloride, evaporated to dryness six times, and recrystallised from methanol after treatment with a little neutral charcoal. The products had the following properties: (*a*) 3β : 24-*Diacetoxy-5α-spirost-24-en-23-one* (from *neo*tigogenin), m. p. 220—226°, $[\alpha]_D$ −95° (Found: C, 70·3; H, 8·7. $C_{31}H_{44}O_7$ requires C, 70·4; H, 8·4%), $\lambda_{max.}$ 242 mμ (log ε 4·0), $\nu_{max.}$ 1770 (vinyl acetate), 1728 (acetate), 1702 and 1668 (αβ-unsaturated ketone), 1250 (acetate), 1198 (vinyl acetate), 765 cm.$^{-1}$; (*b*) (from tigogenin), m. p. 222—226°, $[\alpha]_D$ −95° (Found: C, 70·4; H, 8·4%), $\lambda_{max.}$ 242 mμ (log ε 4·0), $\nu_{max.}$ 1765, 1725, 1700, 1665, 1250, 1197, 762 cm.$^{-1}$.

Reduction of the 23-Oxosapogenin Acetates by Sodium Borohydride.—To the 23-oxosapogenin acetate (100 mg.) in methanol (50 ml.) was added a solution of sodium borohydride (20 mg.) in water (1 ml.) and methanol (4 ml.) and, after the evolution of hydrogen had ceased, the mixture was boiled for 15 min., and poured into water. The solid was collected, washed, dried *in vacuo* over P_2O_5, and recrystallised from acetone–light petroleum (b. p. 80—100°).

3β-*Acetoxy-23-hydroxy-5α-25L-spirostan* has m. p. 188—204°, $[\alpha]_D$ −80° (Found: C, 73·5; H, 9·8. $C_{29}H_{46}O_5$ requires C, 73·4; H, 9·8%), $\nu_{max.}$ 3450, 1725, 1250 cm.$^{-1}$, hydrolysed by ethanolic 5% potassium hydroxide to 3β : 23-*dihydroxy-5α-25L-spirostan*, m. p. 218—230° [from acetone–light petroleum (b. p. 60—80°)], $[\alpha]_D$ −77° (Found: C, 74·6; H, 10·1. $C_{27}H_{44}O_4$ requires C, 74·9; H, 10·3%), $\nu_{max.}$ 3440 cm.$^{-1}$.

3β-*Acetoxy-23-hydroxy-5α-25D-spirostan* has m. p. 203—213°, $[\alpha]_D$ −59° (Found: C, 73·0; H, 9·9%), $\nu_{max.}$ 3400, 1735, 1250 cm.$^{-1}$, and is hydrolysed to 3β : 23-*dihydroxy-5α-25D-spirostan*, m. p. 222—226° [from acetone–light petroleum (b. p. 80—100°)], $[\alpha]_D$ −65° (Found: C, 74·7; H, 9·9%), $\nu_{max.}$ 3300 cm.$^{-1}$.

Dehydrobrominations.—24-Bromo-23-oxo*neo*tigogenin acetate (240 mg.) was boiled under reflux with collidine (20 ml.) for 2 hr. The collidine was then evaporated under reduced pressure and the residue taken up in chloroform, washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water, and dried. Evaporation gave a brown residue which was percolated through neutral alumina in benzene–light petroleum (b. p. 60—80°) (1 : 2), yielding a mixture (199 mg.) of α-bromo-ketone and αβ-unsaturated ketone. This was chromatographed on alumina (Spence Type H); benzene–light petroleum (b. p. 60—80°; 1 : 2) eluted the α-bromo-ketone, and benzene–light petroleum (1 : 1) eluted αβ-unsaturated ketone (58 mg.). Two recrystallisations from methanol gave plates of 3β-*acetoxy-5α-spirost-24-en-23-one*, m. p. 237—246°, $[\alpha]_D$ −84° (Found: C, 73·5; H, 9·1. $C_{29}H_{42}O_5$ requires C, 74·0; H, 9·0%), $\lambda_{max.}$ 233 mμ (log ε 4·1), $\nu_{max.}$ 1732 (acetate), 1682 and 1643 (αβ-unsaturated ketone), 1250 (acetate), 894, 871, 847 cm.$^{-1}$ (trisubstituted double bond).

24-Bromo-23-oxotigogenin acetate (204 mg.) was dehydrobrominated as described above. Chromatography on alumina (Spence Type H) did not completely separate unchanged starting material. The fractions (22 mg.) containing the αβ-unsaturated ketone were recrystallised three times from methanol, to give material (5 mg.) of m. p. 234—236°, $\lambda_{max.}$ 232 mμ (log ε 3·9), $\nu_{max.}$ 1730, 1690, 1645, 1250, 893, 873, 850 cm.$^{-1}$. *X*-Ray diffraction patterns of single crystals of this material, and of 3β-acetoxy-5α-spirost-24-en-23-one described above were similar, but not identical. Further purification was not attempted.

We are indebted to Dr. J. W. Cornforth for many helpful discussions, Dr. C. Djerassi for the optical rotatory dispersion curves, Dr. J. E. Page for infrared absorption spectra of the 24-bromo-23-oxosapogenins in the low-frequency range, Mrs. O. Kennard for the *X*-ray diffraction photographs, and Miss Patricia Dodson for technical assistance.

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[*Received, June 7th*, 1957.]