205. *Some Steroidal 1 : 4-Diene-3 : 11-diones and 1 : 4 : 6-Triene-3 : 11-diones.**

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Hecogenin acetate (IV; R = R′ = H) has been converted into 5α : 25*D*-spirostan-3 : 11-dione (III; R = R′ = H) and thence by the appropriate bromination–dehydrobromination sequences into the corresponding 1-ene (I; R = H, R′ = Br), 4-ene (IX; R = H), 1 : 4-diene (VII; R = H), and 1 : 4 : 6-triene (XI; R = Br).

3β-Acetoxy-5α-pregnane-12 : 20-dione, obtained from hecogenin, has been similarly converted into pregna-1 : 4 : 16-triene-3 : 11 : 20-trione (XVIII).

Attempts to enforce the dienone– or trienone–phenol rearrangement on the above ketones by toluene-*p*-sulphonic acid in acetic anhydride proved unsuccessful.

We were interested in extending the dienone– and trienone–phenol rearrangement to 11-oxo-steroids. To this end we have prepared 25D-spirosta-1 : 4-diene-3 : 11-dione (VII; R′ = H), 23ξ-bromo-25*D*-spirosta-1 : 4 : 6-triene-3 : 11-dione (XI; R′ = Br), and pregna-1 : 4 : 16-triene-3 : 11 : 20-trione (XVIII) from hecogenin.

11α : 23ξ-Dibromohecogenin acetate (IV; R = R′ = Br)[1] was converted into 23ξ-bromo-11β- : 12β-epoxy-5α : 25*D*-spirostan-3β-ol (V)[2,3] by reduction with sodium borohydride and alkaline hydrolysis. Reaction of the epoxide (V) with hydrobromic acid gave the bromohydrin, which was not isolated but was converted directly into 12α : 23ξ-dibromo-5α : 25*D*-spirostan-3 : 11-dione (III; R = R′ = Br) by oxidation with chromic acid. The constitution assigned to the dione (III; R = R′ = Br) was confirmed by its debromination with zinc dust to 5α : 25*D*-spirostan-3 : 11-dione[4] (III; R = R′ = H). Partial debromination with zinc dust in cold benzene–acetic acid gave the 23ξ-monobromo-derivative (III; R = H, R′ = Br) in good yield.

Bromination of the 3 : 11-diones (III; R = R′ = H; R = R′ = Br; and R = H, R′ = Br) was next examined.

5α : 25*D*-Spirostan-3 : 11-dione (III; R = R′ = H) reacted rapidly with one molar equivalent of bromine in acetic acid, to give an inseparable mixture of products. With two molar equivalents, in contrast, a single dibromo-derivative was obtained, which differed from the 12α : 23ξ-dibromo-dione (III; R = R′ = Br). The same dibromo-derivative was also obtained by monobromination of 23ξ-bromo-5α : 25*D*-spirostan-3 : 11-dione (III; R = H, R′ = Br), thereby revealing the presence in it of a 23ξ-bromo-substituent. Its constitution as 2α : 23ξ-dibromo-5α : 25*D*-spirostan-3 : 11-dione (VIII; R = H) followed from its dehydrobromination by boiling collidine to 23ξ-bromo-5α : 25*D*-spirost-1-en-3 : 11-dione (I; R = H, R′ = Br) ($\lambda_{max.}$ 227 mμ), and its conversion by

* Cf. Callow and James (*J.*, 1956, 4744) who have independently reported the conversion of 3β-acetoxy-5α-pregn-16-ene-12 : 20-dione into 5α-pregnane-3 : 11 : 20-trione by an identical route.

[1] Djerassi, Martinez, and Rosenkranz, *J. Org. Chem.*, 1951, **16**, 303; Mueller, Stobaugh and Winniford, *J. Amer. Chem. Soc.*, 1951, **73**, 2400.

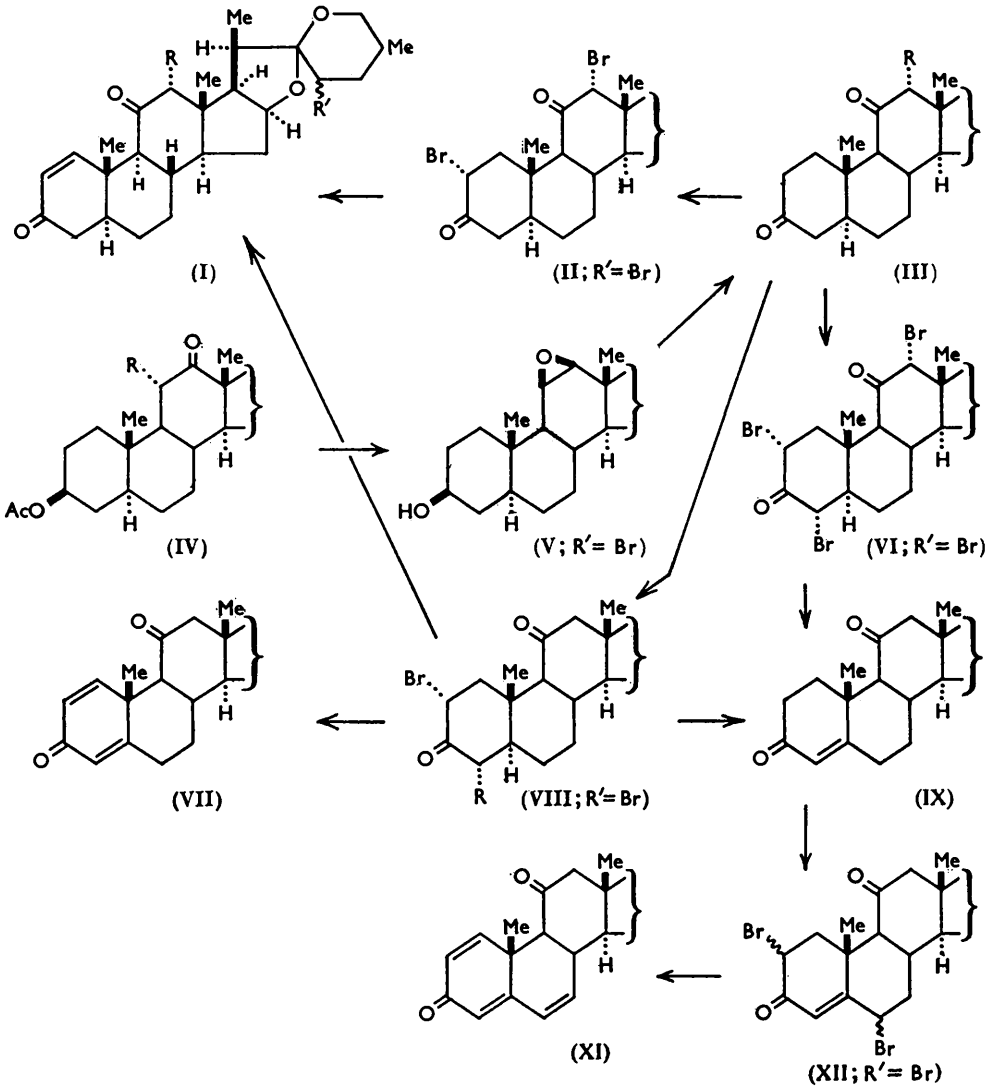
[2] Cornforth, Osbond, and Phillipps, *J.*, 1954, 907.

[3] Schmidlin and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 1241.

[4] Djerassi, Ringold, and Rosenkranz, *J. Amer. Chem. Soc.*, 1951, **73**, 5513.

2 : 4-dinitrophenylhydrazine in acetic acid [5] into 23ξ-bromo-5α : 25*D*-spirost-1-en-3 : 11-dione 2 : 4-dinitrophenylhydrazone ($\lambda_{max.}$ 375 mμ). The α-configuration of the 2-halogen atom is rendered likely by precedent.[6]

Reaction of 12α : 23ξ-dibromo-5α : 25*D*-spirostan-3 : 11-dione (III; R = R′ = Br) with one molar equivalent of bromine in acetic acid led to the formation of 2α : 12α : 23ξ-tribromo-5α : 25*D*-spirostan-3 : 11-dione (II). The constitution assigned to this compound followed from (i) its conversion into 12α : 23ξ-dibromo-5α : 25*D*-spirost-1-en-3 : 11-dione (I; R = R′ = Br) ($\lambda_{max.}$ 225 mμ) by treatment with semicarbazide and



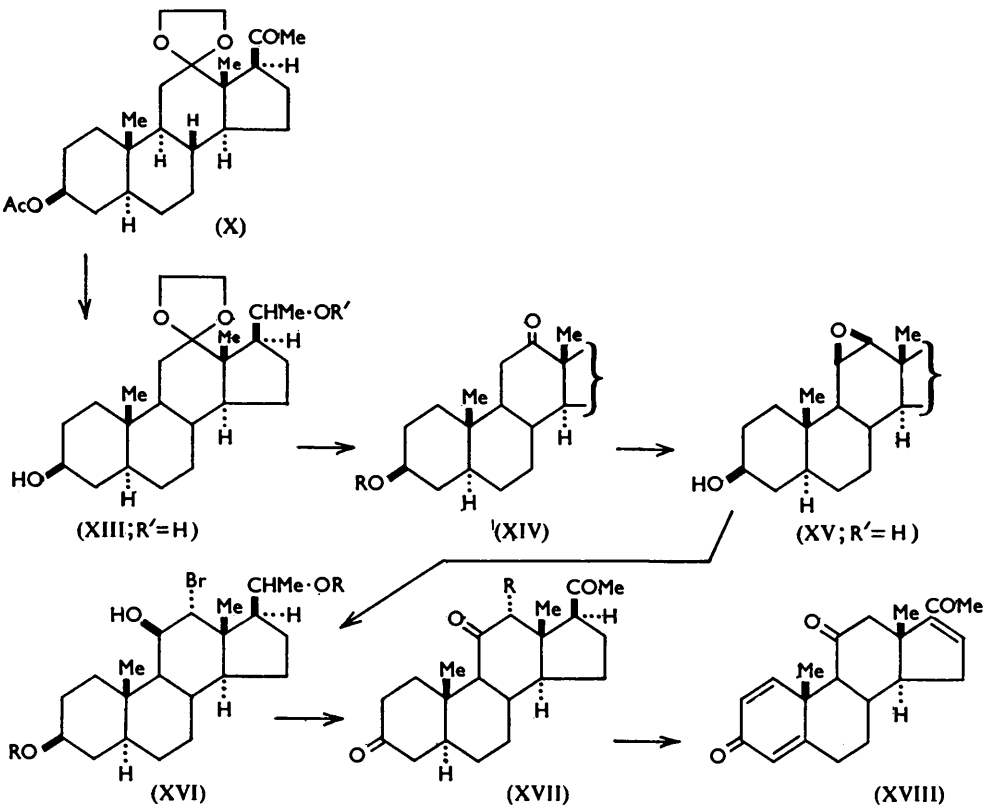
cleavage of the derived semicarbazone with *p*-hydroxybenzaldehyde,[7] and (ii) its conversion into the 2 : 4-dinitrophenylhydrazone of the ketone (I; R = R′ = Br) ($\lambda_{max.}$ 373—375 mμ) by reaction with 2 : 4-dinitrophenylhydrazine. Partial debromination of the dibromide

[5] Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1003.
[6] Jones, Ramsay, Herling, and Dobriner, *ibid.*, 1952, **74**, 2828.
[7] McGuckin and Kendall, *ibid.*, 1952, **74**, 5811; Kritchevsky, Carmaise, and Gallagher, *ibid.*, p. 483.

(I; R = R′ = Br) with zinc dust in cold benzene–acetic acid gave 23ξ-bromo-5α : 25*D*-spirost-1-en-3 : 11-dione (I; R = H, R′ = Br), also prepared (above) by dehydrobromination of the 2α : 23ξ-dibromo-compound (VIII; R = H) with boiling collidine.

Bromination of 23ξ-bromo-5α : 25*D*-spirostan-3 : 11-dione (III; R = H, R′ = Br) with two molar equivalents of bromine, followed immediately by isolation of the products, failed to yield a homogeneous bromo-derivative. After 16—20 hours, however, a green or purple solution was obtained which readily gave a tribromide in good yield. The same compound was subsequently obtained by treating 5α : 25*D*-spirostan-3 : 11-dione (III; R = R′ = H) with three molar equivalents of bromine under similar experimental conditions. The slow appearance of the new tribromide in the bromination liquors is consistent with its formulation as 2α : 4α : 23ξ-tribromo-5α : 25*D*-spirostan-3 : 11-dione (VIII; R = Br) (cf. Jones *et al.*[6] for configuration of the halogen atoms), produced by isomerisation of an intermediate 2 : 2 : 23ξ-tribromide under the influence of the hydrogen bromide present.[8]

Dehydrobromination of the tribromo-derivative (VIII; R = Br) with collidine furnished the required 23ξ-bromo-25*D*-spirosta-1 : 4-dien-3 : 11-dione (VII; R′ = Br),



$\lambda_{max.}$ 239 mμ (in EtOH), characterised by the formation of a 2 : 4-dinitrophenylhydrazone, $\lambda_{max.}$ 389 mμ (in EtOH). Reaction of the tribromo-derivative (VIII; R = Br) with sodium iodide in boiling acetone for 24 hours, followed by gentle de-iodination of the product with zinc dust,[9] furnished 23ξ-bromo-25*D*-spirost-4-en-3 : 11-dione (IX; R′ = Br),

[8] Djerassi and Scholz, *J. Amer. Chem. Soc.*, 1947, **69**, 2404.
[9] Rosenkranz, Mancera, Gatica, and Djerassi, *ibid.*, 1950, **72**, 4077.

$\lambda_{max.}$ 238 mμ (in EtOH), in low yield. The last compound was additionally obtained by dibromination of the 12α : 23ξ-dibromo-derivative (III; R = R′ = Br) under the foregoing experimental conditions, to yield 2α : 4α : 12α : 23ξ-tetrabromo-5α : 25*D*-spirostan-3 : 11-dione (VI), followed by reaction with sodium iodide in acetone and subsequent dehalogenation. *Inter alia*, we examined the action of collidine on the tetrabromo-derivative (VI), but found that, in common with other 12-bromo-11-ones we had previously examined, it gave only an acid-soluble tar.

Dibromination of the ketone (IX; R′ = Br) gave 2 : 6 : 23ξ-tribromo-25*D*-spirost-4-en-3 : 11-dione (XII) (cf. Djerassi *et al.*).[10] Attempts to convert this compound into 23ξ-bromo-25*D*-spirosta-1 : 4 : 6-triene-3 : 11-dione (XI; R′ = Br) by hot collidine gave a product consisting essentially of the required trienedione but contaminated with a more highly brominated impurity as shown by its analysis and ultraviolet absorption spectrum.

Surprisingly, attempted debromination of 23ξ-bromo-25*D*-spirosta-1 : 4-diene-3 : 11-dione (VII; R′ = Br) with zinc in acetic acid gave a non-ketonic product which failed to yield a crystalline fraction after chromatography. Similar reduction of cholesta-1 : 4-dien-3-one gave a gum which furnished *ca.* 10% of a new hydrocarbon, $C_{27}H_{42-44}$, on chromatography. This hydrocarbon showed ultraviolet absorption maxima (in propan-2-ol) at 250, 336, and 352 mμ, but gave evidence of only one ethylenic linkage on perbenzoic acid titration. Its structure remains obscure. No better results were obtained by using zinc dust or a zinc–copper couple in ethanol, whilst catalytic methods led to saturation of the ethylenic linkages. Reductive removal of the 23ξ-bromine atom without concomitant destruction of the 1 : 4-dien-3-one system was ultimately achieved by using sodium iodide in hot acetic acid. In this way the dienone (VII; R′ = Br) was converted into 25*D*-spirosta-1 : 4-diene-3 : 11-dione (VII; R′ = H), $\lambda_{max.}$ 238 mμ (in EtOH). Debromination of the 23ξ-bromo-1 : 4 : 6-triene-3 : 11-dione (XI; R′ = Br) could not be achieved.

The 4-en-3-one (IX; R′ = Br) was similarly reduced to 25*D*-spirost-4-en-3 : 11-dione (IX; R′ = H), $\lambda_{max.}$ 237 mμ (in EtOH), although in this case removal of the halogen atom was also accomplished with zinc–acetic acid.

5α-Pregnane-3 : 11 : 20-trione [11] (XVII; R = H), required for conversion into pregna-1 : 4 : 16-triene-3 : 11 : 20-trione (XVIII), was prepared by converting hecogenin into 11-oxotigogenin and degrading the latter to 3β-acetoxy-5α-pregn-16-ene-11 : 20-dione.[12] Catalytic reduction, hydrolysis and oxidation gave the required trione (XVII; R = H). The overall yield, however, was disappointing. More encouraging results were obtained by effecting removal of the spiroketal side-chain before transference of the 12-oxo-group to the 11-position.

Hecogenin acetate (IV; R = R′ = H) was converted into 3β-acetoxy-5α-pregn-16-ene-12 : 20-dione,[13] and thence into 3β-acetoxy-5α-pregnane-12 : 20-dione.[14] Reaction of the last compound with ethylene glycol and the boron trifluoride–ether complex [15] gave the 12 : 12-ethylenedioxy-derivative (X), which passed into 12 : 12-ethylenedioxy-5α-pregnane-3β : 20ξ-diol (XIII) on reduction with sodium borohydride. Removal of the 12 : 12-ethylenedioxy-group with aqueous acetic acid gave 3β : 20ξ-dihydroxy-5α-pregnan-12-one (XIV; R = R′ = H), converted by acetic anhydride–pyridine in the cold into the 3-monoacetate (XIV; R = Ac; R′ = H) and on prolonged heating into the 3 : 20-diacetate (XIV; R = R′ = Ac).

The monoacetate (XIV; R = Ac, R′ = H) was smoothly converted by 1 molar equivalent of bromine into the 11α-bromo-derivative, admixed with a smaller quantity of the readily removed 11β-bromo-isomer (cf. ref. 2). The diacetate (XIV; R = R′ = Ac),

[10] Djerassi, Rosenkranz, Romo, Kaufmann, and Pataki, *J. Amer. Chem. Soc.*, p. 4534.
[11] Stork, Romo, Rosenkranz, and Djerassi, *ibid.*, 1951, **73**, 3546.
[12] Djerassi, Batres, Romo, and Rosenkranz, *ibid.*, 1952, **74**, 3634.
[13] Wagner, Moore, and Forker, *ibid.*, 1950, **72**, 1856; Cameron, Evans, Hamlet, Hunt, Jones, and Long, *J.*, 1955, 2807.
[14] Adams, Kirk, Patel, Petrow, and Stuart-Webb, *J.*, 1954, 2209.
[15] *Idem*, *ibid.*, p. 2298.

in contrast, gave a lower yield of the 11α-bromo-isomer. Reduction of 3β-acetoxy-11α-bromo-20ξ-hydroxy-5α-pregnan-12-one with sodium borohydride, followed by alkaline hydrolysis, gave 11β : 12β-epoxy-5α-pregnane-3β : 20ξ-diol (XV), smoothly converted by hydrogen bromide into 12α-bromo-5α-pregnane-3β : 11β : 20ξ-triol (XVI; R = H). Chromic acid oxidation of the last compound furnished 12α-bromo-5α-pregnane-3 : 11 : 20-trione (XVII; R = Br), which gave 5α-pregnane-3 : 11 : 20-trione (XVII; R = H) in nearly quantitative yield on reduction with zinc dust in benzene–acetic acid. Tribromination of this product, followed by dehydrobromination of the crude tribromo-derivative with collidine (cf. Rubin *et al.*) [16] gave the required pregna-1 : 4 : 16-triene-3 : 11 : 20-trione, $\lambda_{max.}$ 236 mμ (in Pr^{i}OH), characterised as the bisdinitrophenylhydrazone, $\lambda_{max.}$ 385—386 mμ (in Pr^{i}OH).

The foregoing dienic ketones failed to undergo the dienone–heterophenol rearrangement [17] under the usual conditions of heating with toluene-*p*-sulphonic acid and acetic anhydride. No better result was obtained with the trienic ketone, there being no evidence of the normal trienone–phenol rearrangement.[18]

This observation argues for a lower reactivity of the 1 : 4-dien-3-one system owing, presumably, to the (−*I*) inductive effect of the 11-oxo-group. This view is supported by comparison of the ultraviolet absorption maxima of the above dienones and trienones with their 11-deoxy-analogues: a significant hypsochromic shift associated with the presence of the 11-oxo-group in the molecule is clearly to be seen.

Experimental

Optical rotations were measured on $CHCl_3$ solutions in a 1 dm. tube unless otherwise stated. Ultraviolet absorption spectra were kindly determined by Mr. M. Davies, B.Sc.

12α : 23ξ-*Dibromo*-5α : 25D-*spirostan*-3 : 11-*dione* (III; R = R′ = Br).—11α : 23ξ-Dibromohecogenin acetate (IV; R = R′ = Br) [1] was converted into 23ξ-bromo-11β : 12β-epoxy-5α : 25*D*-spirostan-3β-ol (V) essentially by the method of Cornforth *et al.*[2] The bromo-compound (45 g.) in dioxan (450 ml.) was treated with 48% aqueous hydrobromic acid (67·5 ml.) in dioxan (135 ml.) and water (5 ml.). After 16 hr. at room temperature the mixture was poured into water (2 l.), and the product isolated with methylene chloride (3 × 300 ml.), to which was then added with vigorous stirring a solution of chromium trioxide (45 g.) in water (135 ml.) and acetic acid (270 ml.). Stirring was continued for 7 hr. after which the mixture was poured into water and the product isolated from the non-aqueous layer. Purification from ethanol gave 12α : 23ξ-*dibromo*-5α : 25*D*-*spirostan*-3 : 11-*dione*, needles, m. p. 209°, $[\alpha]_D^{27}$ −69° (*c* 0·52) (Found: C, 55·4; H, 6·7; Br, 27·2. $C_{27}H_{38}O_4Br_2$ requires C, 55·3; H, 6·5; Br, 27·3%).

23ξ-*Bromo*-5α : 25D-*spirostan*-3 : 11-*dione* (III; R = H, R′ = Br).—The foregoing compound (25 g.) in benzene (500 ml.) and acetic acid (250 ml.) was stirred and treated with zinc dust (50 g.) added in four portions at intervals of 15 min. at <30°. After a further 15 min. the mixture was filtered, the solids were washed with acetic acid (50 ml.), and the filtrate and washings poured into water. The benzene layer yielded 23ξ-*bromo*-5α : 25D-*spirostan*-3 : 11-*dione*, plates, m. p. 232—234°, $[\alpha]_D^{24}$ −19° (*c* 0·41) (Found: C, 63·5; H, 7·7; Br, 15·3. $C_{27}H_{39}O_4Br$ requires C, 63·8; H, 7·7; Br, 15·7%), after crystallisation from chloroform–ethanol.

5α : 25D-*Spirostan*-3 : 11-*dione* (III; R = R′ = H).—12α : 23ξ-Dibromo-5α : 25*D*-spirostan-3 : 11-dione (5 g.) in acetic acid (50 ml.) and sodium acetate (10 g.) was heated under reflux with zinc dust (20 g.) for 1·5 hr. The product, isolated as above, crystallised from aqueous ethanol, to give 5α : 25*D*-spirostan-3 : 11-dione, needles, m. p. 237—239°, $[\alpha]_D^{24}$ −19° (*c* 0·57) (Found: C, 75·6; H, 9·4. Calc. for $C_{27}H_{40}O_4$: C, 75·7; H, 9·4%).

2α : 23ξ-*Dibromo*-5α : 25D-*spirostan*-3 : 11-*dione* (VIII; R = H).—(*a*) 5α : 25*D*-Spirostan-3 : 11-dione (4 g.) in acetic acid (200 ml.) was treated dropwise with bromine in acetic acid (17·5 ml. of 1·08M). 2α : 23ξ-*Dibromo*-5α : 25D-*spirostan*-3 : 11-*dione* was isolated with methylene chloride as needles, m. p. 214—216°, $[\alpha]_D^{25}$ −22° (*c* 0·448) (Found: C, 55·9; H, 6·8; Br, 28·6.

[16] Rubin, Wishinsky, and Bompard, *J. Amer. Chem. Soc.*, 1951, **73**, 2338.
[17] Woodward and Singh, *ibid.*, 1950, **72**, 494; Dreiding and Voltman, *ibid.*, 1954, **76**, 537.
[18] Djerassi and Rosenkranz, *J. Org. Chem.*, 1950, **15**, 896; Djerassi, Rosenkranz, Romo, Pataki, and Kaufmann, *J. Amer. Chem. Soc.*, 1950, **72**, 4540.

$C_{27}H_{38}O_4Br_2$ requires C, 55·3; H, 6·5; Br, 29·3%), after crystallisation from methylene chloride–methanol. (*b*) 23ξ-Bromo-5α : 25*D*-spirostan-3 : 11-dione (1 g.) in acetic acid (50 ml.) was treated with bromine in acetic acid (8·3 ml. of 0·24M), to give the dibromo-derivative, m. p. 214—216°, alone or on admixture with a sample prepared as under (*a*).

23ξ-*Bromo*-5α : 25D-*spirost*-1-*en*-3 : 11-*dione* (I; R = H, R′ = Br).—(*a*) 2α : 23ξ-Dibromo-5α : 25D-spirostan-3 : 11-dione (2 g.) in collidine (16 ml.) was heated under reflux in nitrogen for 1 hr. The product was isolated with benzene, and the benzene solution was percolated through chromatographic alumina (10 g.; B.D.H.). Purification of the product from methylene chloride–methanol gave 23ξ-*bromo*-5α : 25D-*spirost*-1-*en*-3 : 11-*dione*, plates, m. p. 226—227°, $[\alpha]_D^{25}$ +7° (*c* 0·640), $\lambda_{max.}$ 227 mμ (log ε 4·00 in EtOH) (Found : C, 64·4; H, 7·4; Br, 15·4. $C_{27}H_{37}O_4Br$ requires C, 64·2; H, 7·4; Br, 15·8%).

(*b*) 12α : 23ξ-Dibromo-5α : 25*D*-spirost-1-en-3 : 11-dione (150 mg.) (see below) in acetic acid (3 ml.) and benzene (5 ml.) was shaken with zinc dust (1 g.) at room temperature for ½ hr. The product, after purification from methylene chloride–methanol, was identified with the preceding compound.

(*c*) 2α : 23ξ-Dibromo-5α : 25*D*-spirostan-3 : 11-dione (250 mg.) in acetic acid (10 ml.) and chloroform (3 ml.) was heated with 2 : 4-dinitrophenylhydrazine (150 mg.) and sodium acetate (60 mg.) at 60° under nitrogen for ½ hr. After removal of the chloroform, the mixture was allowed to cool, 23ξ-*bromo*-5α : 25D-*spirost*-1-*en*-3 : 11-*dione* 3-(2 : 4-*dinitrophenylhydrazone*) separating in orange-red leaflets, m. p. 255—258°, $\lambda_{max.}$ 375 mμ (log ε 4·49 in $CHCl_3$) (Found : N, 8·4; Br, 10·9. $C_{33}H_{41}O_7N_4Br$ requires N, 8·2; Br, 11·6%), after crystallisation from chloroform–ethyl acetate.

2α : 12α : 23ξ-*Tribromo*-5α : 25D-*spirostan*-3 : 11-*dione* (II), needles, m. p. 204—208°, $[\alpha]_D^{23}$ −71° (*c* 0·602) (Found : C, 48·8; H, 5·7; Br, 35·8. $C_{27}H_{37}O_4Br_3$ requires C, 48·7; H, 5·6; Br, 36·0%), after crystallisation from methylene chloride–methanol, was prepared by treating 12α : 23ξ-dibromo-5α : 25*D*-spirostan-3 : 11-dione (2 g.) in acetic acid (50 ml.) with bromine in acetic acid (16 ml. of 0·214M) and isolating the product with methylene chloride.

12α : 23ξ-*Dibromo*-5α : 25D-*spirost*-1-*en*-3 : 11-*dione* (I; R = R′ = Br).—The foregoing compound (250 mg.), semicarbazide hydrochloride (50 mg.), and sodium acetate (40 mg.) in 90% acetic acid (10 ml.) were heated on the steam-bath under nitrogen for 1 hr. A solution of *p*-hydroxybenzaldehyde (2·5 g.) and sodium acetate (40 mg.) in 50% acetic acid (20 ml.) was then added and heating continued for 2 hr. The product, isolated with ether, was purified from methylene chloride–methanol, to give 12α : 23ξ-*dibromo*-5α : 25D-*spirost*-1-*en*-3 : 11-*dione*, plates, m. p. 225°, $[\alpha]_D^{24}$ −57° (*c* 0·856), $\lambda_{max.}$ 225 mμ (log ε 4·06 in EtOH) (Found : Br, 28·3. $C_{27}H_{36}O_4Br_2$ requires Br, 27·4%).

The 3-(2 : 4-*dinitrophenylhydrazone*), m. p. 245—247°, $\lambda_{max.}$ 373—375 mμ (log ε 4·46 in PrⁱOH) (Found : Br, 20·2; N, 6·8. $C_{33}H_{40}O_7N_4Br_2$ requires Br, 20·9; N, 7·3%), from ethyl acetate–chloroform, was obtained by heating the tribromo-derivative (II) (250 mg.), 2 : 4-dinitrophenylhydrazine (150 mg.), anhydrous sodium acetate (60 mg.), acetic acid (7 ml.), and chloroform (4 ml.) at 60° under nitrogen for ½ hr.

2α : 4α : 23ξ-*Tribromo*-5α : 25D-*spirostan*-3 : 11-*dione* (VIII; R = Br).—23ξ-Bromo-5α : 25*D*-spirostan-3 : 11-dione (15 g.) in acetic acid (1 l.) was treated with bromine in acetic acid (57·5 ml. of 1·05M) during ½ hr., after which a 50% (w/v) solution (10 ml.) of hydrogen bromide in acetic acid was added. After being kept overnight at room temperature the blue solution was poured into water, and the product isolated with methylene chloride. Trituration with ether, followed by crystallisation from methylene chloride–methanol gave 2α : 4α : 23ξ-*tribromo*-5α : 25D-*spirostan*-3 : 11-*dione*, plates, m. p. 202—205°, $[\alpha]_D^{22}$ −21° (*c* 0·592) (Found : C, 49·1; H, 5·6; Br, 35·1. $C_{27}H_{37}O_4Br_3$ requires C, 48·7; H, 5·6; Br, 36·0%). The same compound was also obtained by treating 5α : 25*D*-spirostan-3 : 11-dione (4·0 g.) in acetic acid (200 ml.) with bromine in acetic acid (26·8 ml. of 1·05M) overnight at room temperature.

23ξ-*Bromo*-25D-*spirosta*-1 : 4-*diene*-3 : 11-*dione* (VII; R′ = Br).—The foregoing compound (8·5 g.) in collidine (60 ml.) was heated under reflux under nitrogen for 1·5 hr. The product in benzene solution was percolated through chromatographic alumina (30 g.; B.D.H.) and subsequently purified from methylene chloride–methanol, to give 23ξ-*bromo*-25D-*spirosta*-1 : 4-*diene*-3 : 11-*dione*, leaflets, m. p. 216°, $[\alpha]_D^{25}$ +30° (*c* 0·439), $\lambda_{max.}$ 239 mμ (log ε 4·12 in PrⁱOH) (Found : C, 64·1; H, 6·8; Br, 16·3. $C_{27}H_{35}O_4Br$ requires C, 64·4; H, 7·0; Br, 15·9%). The 3-(2 : 4-*dinitrophenylhydrazone*) formed red plates, m. p. 257—260° (decomp.), $\lambda_{max.}$ 389 mμ (log ε 4·49 in PrⁱOH) (Found : N, 8·0; Br, 11·6. $C_{33}H_{39}O_6N_4Br$ requires N, 8·4; Br, 12·0%).

2α : 4α : 12α : 23ξ-*Tetrabromo*-5α : 25D-*spirostan*-3 : 11-*dione*, leaflets, m. p. 197—202°, $[\alpha]_D^{25}$ −70° (*c* 0·364) (Found: C, 43·6; H, 4·9; Br, 42·7. $C_{27}H_{36}O_4Br_4$ requires C, 43·6; H, 4·9; Br, 43·0%), after crystallisation from methylene chloride–methanol, was obtained by treating 12α : 23ξ-dibromo-5α : 25*D*-spirostan-3 : 11-dione (10 g.) in acetic acid (250 ml.) with bromine in acetic acid (31·7 ml. of 1·08M) with stirring during ½ hr. and then leaving the mixture overnight at room temperature.

23ξ-*Bromo*-25D-*spirost*-4-*en*-3 : 11-*dione* (IX; R′ = Br).—(*a*) 2α : 4α : 12α : 23ξ-Tetrabromo-5α : 25*D*-spirostan-3 : 11-dione (9·15 g.) in dry acetone (300 ml.) and sodium iodide (20 g.) were heated under reflux under nitrogen for 24 hr. The product was isolated with methylene chloride, dissolved in benzene (100 ml.) and acetic acid (50 ml.), and stirred with zinc dust (20 g.) for ½ hr. at room temperature. It was then chromatographed in benzene–light petroleum (200 ml.; 1 : 4) on alumina (100 g., B.D.H.). Elution with benzene–light petroleum (1 : 1) gave 2·35 g. of 23ξ-bromo-5α : 25*D*-spirostan-3 : 11-dione. Elution with benzene and benzene–ether (4 : 1) yielded 23ξ-*bromo*-25D-*spirost*-4-*en*-3 : 11-*dione*, needles, m. p. 217—219°, $[\alpha]_D^{26}$ +65° (*c* 0·742), $\lambda_{max.}$ 238 mμ (log ε 4·1 in EtOH) (Found: C, 64·2; H, 7·4; Br, 15·9. $C_{27}H_{37}O_4Br$ requires C, 64·1; H, 7·4; Br, 15·8%), after crystallisation from ethanol.

(*b*) 2α : 4α : 23ξ-Tribromo-5α : 25*D*-spirostan-3 : 11-dione (16·3 g.) and sodium iodide (33 g.) in dry acetone (330 ml.) were refluxed under nitrogen for 21 hr., The product, in benzene, was chromatographed on alumina (180 g.). Elution with benzene–light petroleum (1 : 1) gave 7 g. of (ultraviolet light) spectroscopically transparent material. Elution with benzene–ether gave the foregoing ketone, m. p. 216—219°, not depressed on admixture with a sample prepared as under (*a*).

25D-*Spirost*-4-*en*-3 : 11-*dione* (IX; R′ = H).—(*a*) 23ξ-Bromo-25*D*-spirost-4-en-3 : 11-dione (560 mg.) in acetic acid (12·5 ml.) containing sodium acetate (2·5 g.) was heated with zinc dust (2 g.) under reflux for 2 hr. 25D-*Spirost*-4-*en*-3 : 11-*dione*, isolated with benzene, formed plates, m. p. 212—215°, $[\alpha]_D^{26}$ +60° (*c* 0·568), $\lambda_{max.}$ 237 mμ (log ε 4·10 in EtOH) (Found: C, 76·4; H, 8·8. $C_{27}H_{38}O_4$ requires C, 76·1; H, 9·0%), from acetone–hexane.

(*b*) 23ξ-Bromo-25*D*-spirost-4-en-3 : 11-dione (1 g.) and sodium iodide (1 g.) in acetic acid (15 ml.) were heated under nitrogen on a steam-bath for 20 hr. The solution was poured into excess of sodium thiosulphate solution, and the product isolated with benzene and purified from acetone–hexane, to give 25*D*-spirost-4-en-3 : 11-dione, m. p. 211—215°, not depressed on admixture with a sample prepared as under (*a*).

2ξ : 6ξ - 23ξ-*Tribromo*-25D-*spirost*-4-*en*-3 : 11-*dione* (XII).—23ξ-Bromo-25*D*-spirost-4-en-3 : 11-dione (2 g.), suspended in dry ether (120 ml.), was treated dropwise with bromine in acetic acid (7·6 ml. of 1·05M) at 0—5°. After ½ hr. the ether was removed under reduced pressure at 20°, methanol (20 ml.) was added, and the separated solids were collected after ½ hr. Purification from methylene chloride–methanol gave 2ξ : 6ξ : 23ξ-*tribromo*-25D-*spirost*-4-*en*-3 : 11-*dione*, leaflets, m. p. 209—210°, $[\alpha]_D^{24}$ +8° (*c* 0·522), $\lambda_{max.}$ 236—237 mμ (log ε 4·0 in Pr^iOH) (Found: C, 49·5; H, 5·4; Br, 36·8. $C_{27}H_{35}O_4Br_3$ requires C, 48·9; H, 5·3; Br, 36·2%).

23ξ-*Bromo*-25D-*spirosta*-1 : 4 : 6-*triene*-3 : 11-*dione* (XI; R′ = Br).—The foregoing compound (1 g.) in collidine (10 ml.) was heated under reflux under nitrogen for 1½ hr. The product, in benzene, was percolated through alumina (7 g.) and then purified from acetone–hexane, to give 23ξ-*bromo*-25D-*spirosta*-1 : 4 : 6-*triene*-3 : 11-*dione*, leaflets, m. p. 200—204°, $[\alpha]_D^{24}$ +51° (*c* 0·24), $\lambda_{max.}$ 225 (log ε 4·03), 269 (log ε 3·87) and 305 mμ (log ε 3·93) in Pr^iOH (Found: C, 61·7; H, 6·5; Br, 20·8. $C_{27}H_{33}O_4Br$ requires C, 64·6; H, 6·6; Br, 16·0%).

Debromination of 23ξ-*bromo*-25D-*spirosta*-1 : 4-*diene*-3 : 11-*dione with Zinc Dust*.—This dione (500 mg.) in acetic acid (10 ml.), sodium acetate (2 g.; anhyd.) and zinc dust (2 g.) were boiled under reflux for 1·5 hr. (cf. Cornforth *et al.*[2]). The product, isolated by means of ether, was a bromine-free gum which gave no crystalline material on chromatography over alumina (10 g.) and failed to form a 2 : 4-dinitrophenylhydrazone.

25D-*Spirosta*-1 : 4-*diene*-3 : 11-*dione* (VII; R′ = H), prepared by heating 23ξ-bromo-25*D*-spirosta-1 : 4-diene-3 : 11-dione (VII; R′ = Br) (5 g.) and sodium iodide (10 g.) in acetic acid (75 ml.) under nitrogen on a steam-bath for 30 hr., formed plates, m. p. 240—243°, $[\alpha]_D^{15}$ +36° (*c* 0·926), $\lambda_{max.}$ 238 mμ (log ε 4·15 in Pr^iOH) (Found: C, 76·1; H, 8·5. $C_{27}H_{36}O_4$ requires C, 76·4; H, 8·6%), after crystallisation from methylene chloride–methanol.

Reduction of Cholesta-1 : 4-*dien*-3-*one with Zinc and Acetic Acid*.—Cholesta-1 : 4-dien-3-one (1 g.) was reduced under reflux with zinc dust (2 g.) in acetic acid (10 ml.) containing sodium acetate (2 g.). The product, isolated with ether, was chromatographed in benzene on alumina

(30 g.). Elution with light petroleum, followed by purification from the same solvent, yielded a *hydrocarbon*, m. p. 190—196°, $\lambda_{max.}$ 250 ($E^{1\%}_{1cm.}$ 116), 336 ($E^{1\%}_{1cm.}$ 264) and 352 mμ ($E^{1\%}_{1cm.}$ 265) in hexane (Found : C, 87·8; H, 11·5%).

3β-*Acetoxy*-12 : 12-*ethylenedioxy*-5α-*pregnan*-20-*one* (X).—Finely powdered 3β-acetoxy-5α-pregnane-12 : 20-dione (82 g.) in freshly distilled ethylene glycol (600 ml.) was treated with boron trifluoride–ether complex (120 ml.) for 72 hr. at room temperature with occasional swirling. The product, in pyridine (200 ml.), was treated overnight at room temperature with acetic anhydride (500 ml.) and recovered in benzene and crystallised from methanol. 3β-*Acetoxy*-12 : 12-*ethylenedioxy*-5α-*pregnan*-20-*one* formed leaflets, m. p. 159—162°, $[\alpha]_D^{25}$ +99° (*c* 0·624) (Found : C, 72·4; H, 8·9. $C_{25}H_{36}O_5$ requires C, 71·8; H, 9·1%), after crystallisation from methanol.

12 : 12-*Ethylenedioxy*-5α-*pregnane*-3β : 20ξ-*diol* (XIII), prepared by reducing the foregoing compound (14·8 g.) in methanol (1·5 l.) with sodium hydroxide (7·5 g.) and sodium borohydride (3 g.) in 50% aqueous methanol (300 ml.) at room temperature for 60 hr., formed prisms, m. p. 198—200°, $[\alpha]_D^{25}$ +40° (*c* 1·060) (Found : C, 73·2; H, 10·0. $C_{23}H_{38}O_4$ requires C, 73·0; H, 10·1%), from acetone.

3β : 20ξ-*Dihydroxy*-5α-*pregnan*-12-*one* (XIV; R = R′ = H), prepared by heating the foregoing compound (22·5 g.) in 90% acetic acid (450 ml.) on the steam-bath for 1 hr., formed rectangular plates, m. p. 230—233°, $[\alpha]_D^{25}$ +91° (*c* 0·701) (Found : C, 75·3; H, 10·4. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·2%), from methylene chloride–ethyl acetate.

Acetylation of the foregoing compound (28·4 g.) in pyridine (200 ml.) with acetic anhydride (100 ml.) at room temperature overnight gave 3β-*acetoxy*-20ξ-*hydroxy*-5α-*pregnan*-12-*one*, prisms, m. p. 198—201°, $[\alpha]_D^{22}$ +71° (*c* 0·485) (Found : C, 73·8; H, 9·7. $C_{23}H_{36}O_4$ requires C, 73·5; H, 9·6%), after crystallisation from acetone–hexane. The mother-liquors were taken to dryness and the residue extracted several times with light petroleum under reflux. The insoluble fraction yielded a further quantity of the 3-monoacetate. The soluble fraction, after purification from aqueous methanol, yielded 3β : 20ξ-*diacetoxy*-5α-*pregnan*-12-*one*, leaflets, m. p. 135—138°, $[\alpha]_D^{26}$ +96° (*c* 0·576) (Found : C, 71·6; H, 8·9. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·1%). The last compound formed the sole product when the diol (1 g.) in acetic anhydride (5 ml.) and pyridine (3 ml.) was heated on the steam-bath for 16 hr.

3β-*Acetoxy*-11α-*bromo*-20ξ-*hydroxy*-5α-*pregnan*-12-*one*.—3β-Acetoxy-20ξ-hydroxy-5α-pregnan-12-one (10 g.) in acetic acid (400 ml.) at 30° was treated with 3 drops of a 50% solution of hydrogen bromide in acetic acid, followed by bromine in acetic acid (24·5 ml. of 1·1M), added dropwise over 30 min. After a further 10 min. the product was isolated with methylene chloride and purified from ethyl acetate. 3β-*Acetoxy*-11α-*bromo*-20ξ-*hydroxy*-5α-*pregnan*-12-*one* formed prisms, m. p. 164—167°, $[\alpha]_D^{22}$ +12° (*c* 0·412) (Found : C, 61·0; H, 7·9; Br, 17·5. $C_{23}H_{35}O_4Br$ requires C, 60·7; H, 7·8; Br, 17·5%).

11β : 12β-*Epoxy*-5α-*pregnane*-3β : 20ξ-*diol* (XV).—The 11α-bromo-ketone (6 g.) in ethanol (900 ml.) was treated with sodium hydrogen carbonate (600 mg.) and sodium borohydride (600 mg.) in water (30 ml.) for 2 hr. with stirring. Potassium hydroxide (9 g.) was then added and stirring continued for 4 hr. The product, 11β : 12β-*epoxy*-5α-*pregnane*-3β : 20ξ-*diol*, m. p. 218—221°, $[\alpha]_D^{24}$ +34° (*c* 0·745), crystallised from aqueous methanol (Found : C, 75·6; H, 10·3. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·2%).

12α-*Bromo*-5α-*pregnane*-3β : 11β : 20ξ-*triol* (XVI; R = H), needles, m. p. 210—211°, $[\alpha]_D^{26}$ +29° (*c* 0·448 in EtOH) (Found : C, 60·9; H, 8·4; Br, 19·1. $C_{21}H_{35}O_3Br$ requires C, 60·7; H, 8·5; Br, 19·2%), after crystallisation from aqueous methanol, was prepared by treating the foregoing compound (3·4 g.) in dioxan (70 ml.) with 48% hydrobromic acid (5 ml.) in dioxan (10 ml.) and leaving the mixture at room temperature overnight. The *diacetate* separated from methylene chloride–methanol in flattened rods, m. p. 216—218°, $[\alpha]_D^{23}$ +54° (*c* 0·664) (Found : C, 59·8; H, 7·6; Br, 16·3. $C_{25}H_{39}O_5Br$ requires C, 60·1; H, 7·9; Br, 16·0%).

12α-*Bromo*-5α-*pregnane*-3 : 11 : 20-*trione* (XVII; R = Br).—The foregoing compound (2 g.) in methylene chloride (30 ml.) was treated below 25° with vigorous stirring with chromic acid (3 g.) in water (12 ml.) and acetic acid (12 ml.) during ½ hr. Stirring was maintained for a further 4½ hr., after which the product was isolated with methylene chloride and purified from aqueous acetone. The *trione* formed thick needles, m. p. 178—180°, $[\alpha]_D^{25}$ +2° (*c* 0·889) (Found : C, 61·9; H, 7·1; Br, 19·3. $C_{21}H_{29}O_3Br$ requires C, 61·6; H, 7·1; Br, 19·5%).

5α-Pregnane-3 : 11 : 20-trione (XVII; R = H), m. p. 216—218°, alone or on admixture with an authentic sample, $[\alpha]_D^{23}$ +133° (*c* 0·748) (Found : C, 76·5; H, 9·1. Calc. for $C_{21}H_{30}O_3$

C, 76·3; H, 9·1%), was prepared by stirring the foregoing compound (6·25 g.) in benzene (60 ml.) and acetic acid (100 ml.) with zinc dust (10 g. added in 3 portions at intervals of ½ hr.) for a total of 1 hr.

Pregna-1 : 4 : 16-*triene*-3 : 11 : 20-*trione* (XVIII).—The foregoing compound (1·5 g.) in acetic acid (50 ml.) was treated dropwise with bromine in acetic acid (13 ml.; 1·05M). After 20 hr. at room temperature the product was isolated with ether and then heated under reflux with collidine for 1½ hr. under nitrogen. The resulting material, in benzene–light petroleum, was chromatographed on alumina (16 g.). After elution with benzene–light petroleum, elution with benzene and benzene–ether (1 : 1) gave *pregna*-1 : 4 : 16-*triene*-3 : 11 : 20-*trione*, yellow leaflets, m. p. 237—241°, $[\alpha]_D^{25}$ +23° (*c* 0·644), $\lambda_{max.}$ 236 mμ (log ε 4·38 in EtOH) (Found: C, 77·2; H, 7·5. $C_{21}H_{24}O_3$ requires C, 77·7; H, 7·5%), after crystallisation from acetone–hexane.

The 3 : 20-*bis*-(2 : 4-*dinitrophenylhydrazone*) formed plates, m. p. 190°, $\lambda_{max.}$ 385—386 mμ (log ε 4·7 in EtOH) (Found: N, 15·8; $C_{33}H_{32}O_9N_8$ requires N, 16·4%).

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