927. *By-ways of Synthesis of Cortisone from Hecogenin. Part II.*[1] *A Route to* 11-*Oxygenated Compounds through* 3β : 20β-*Diacetoxy*-11-*bromo*allo*pregnan*-12-*one.*

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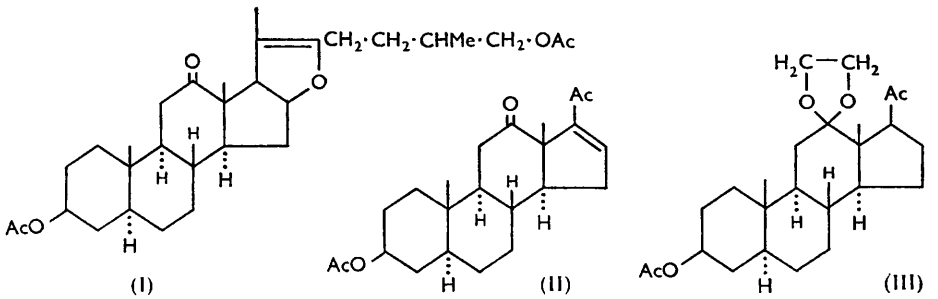
3β-Acetoxy*allo*pregn-16-ene-12 : 20-dione (II), obtained by degradation of ψ-hecogenin diacetate, is reduced to 3β-acetoxy*allo*pregnane-12 : 20-dione which forms a 12 : 12-ethylenedioxy-compound. Selective reduction at $C_{(20)}$ can then be carried out and 3β : 20β-diacetoxy*allo*pregnan-12-one can be monobrominated at $C_{(11)}$ and, by applying the series of reactions used previously with a 12-oxo-sapogenin, *allo*pregnane-3 : 11 : 20-trione, an intermediate in the synthesis of cortisone, is prepared.

As we explained in Part I,[1] the synthetical pathway from hecogenin to cortisone might, at least in theory, be traversed by taking the stages in different orders. In particular, the introduction of oxygen at $C_{(11)}$, previously carried out at the sapogenin stage with hecogenin, might, it was thought, be done after removal of the side chain. The diketone, 3β-acetoxy-*allo*pregn-16-ene-12 : 20-dione, obtained by degradation of ψ-hecogenin diacetate (I), or the *allo*pregnanedione derived from it, have obviously the disadvantage of possessing two activated centres. Nevertheless it was found possible to protect the 12-oxo-group as an ethylene ketal (III) and then to reduce the 20-oxo-group, thus obtaining a 12-ketone which can be brominated on $C_{(11)}$ and converted into an 11-ketone by reactions previously applied at the sapogenin stage.[2]



(I) (II) (III)

Several investigations were, however, necessary before this fairly direct route was completed. Initially, attempts were made to reduce selectively the 20-oxo-group in 3β-acetoxy*allo*pregn-16-ene-12 : 20-dione (II). These were unsuccessful. Hydrogenation with a palladium, platinum, or nickel catalyst in neutral solution reduced only the double bond: with a platinum catalyst in acid solution both carbonyl groups were reduced. Although zinc and acetic acid have been reported [3,4] to reduce the 20-oxo-group in similar compounds, in our experiments only the 16 : 17-double bond was reduced.

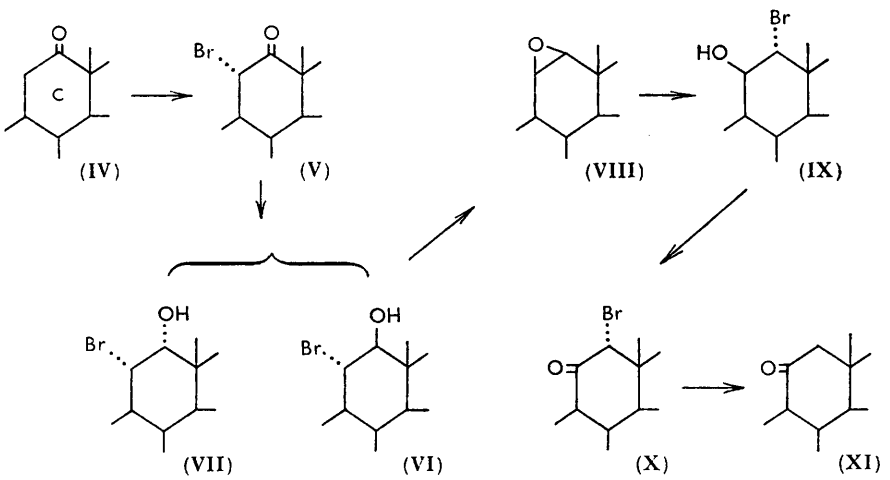
Bromination of the saturated diketone did not lead to a useful result. As much as three atomic proportions of bromine could be introduced into the molecule; one equivalent of bromine gave an approximately monobrominated product, probably not homogeneous. As on treatment with collidine this yielded mainly 3β-acetoxy*allo*pregn-16-ene-12 : 20-dione, bromination had apparently taken place predominantly at $C_{(17)}$.

These results led to an investigation of means of protecting one ketone group before bromination. 3β-Acetoxy*allo*pregnane-12 : 20-dione reacted with ethylene glycol to yield a monoketal. This could be brominated, but only with simultaneous hydrolysis of the ketal group, and the product was apparently the unpurifiable 17-bromo-derivative

[1] Part I, preceding paper.
[2] Cornforth, Osbond, and Phillipps, *J.*, 1954, 907; cf. Schmidlin and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 1241.
[3] Ercoli and de Ruggieri, *Farmaco* (*sci.*), 1952, **7**, 11.
[4] Nes and Mason, *J. Amer. Chem. Soc.*, 1951, **73**, 4765.

previously obtained. The ketal was at first assumed to be the 20 : 20-ethylenedioxy-compound, but it was soon clear that this was not so. Reduction by the Wolff–Kishner reaction yielded 3β-hydroxy*allo*pregnan-12-one, the constitution of which was deduced primarily from the fact that it was not identical with the known 3β-hydroxy*allo*pregnan-20-one. Reduction with lithium aluminium hydride yielded 12 : 12-ethylenedioxy*allo*-pregnane-3β : 20β-diol (for assignment of configuration at $C_{(20)}$ cf. Klyne [5]), hydrolysed to 3β : 20β-dihydroxy*allo*pregnan-12-one. In this case also the constitution was deduced from its difference from 3β : 12β-dihydroxy*allo*pregnan-20-one, which was prepared from hecogenin through the stages rockogenin, ψ-rockogenin triacetate, and 3β : 12β-diacetoxy-*allo*pregn-16-en-20-one. Positive proof of the formation of the 12-ethylene ketal from the 12 : 20-diketone is, of course, provided by the preparation of the 11-oxo-compounds described below. The observation by Adams *et al.*[6], published after the present work had been completed, that 17α-hydroxy*allo*pregnane-12 : 20-dione undergoes ethylene ketal formation exclusively at $C_{(12)}$ is in accord with our conclusion.

3β : 20β-Dihydroxy*allo*pregnan-12-one, now an accessible substance, thus provides a suitable starting point for bromination and ultimately introduction of oxygen at $C_{(11)}$. Surprisingly, the substance itself was inert towards bromine under the usual conditions. This may perhaps be due to interaction of the groups at $C_{(12)}$ and $C_{(20)}$. Infrared absorption indicates hydrogen-bonding in the diol and 3β-monoacetate but not in the diacetate. It



was found that the 3β : 20β-diacetate (IV) reacted readily with bromine to form a mono-bromo-compound, 3β : 20β-diacetoxy-11-bromo*allo*pregnan-12-one (V), which was reduced by sodium borohydride to a complex mixture, of which the 11α-bromo-12β-hydroxy- and the 11α-bromo-12α-hydroxy-compound (VI and VII) were major constituents. The former reacted with alkali to give the 11β : 12β-epoxide (VIII); the latter, under similar conditions, gave the original 12-ketone. The 11β : 12β-epoxide, or its acetate, was converted, by way of intermediates (IX and X) which were not completely characterised, into the known *allo*pregnane-3 : 11 : 20-trione (XI), an intermediate in cortisone synthesis, the series of reactions being essentially that described by Cornforth *et al.* and by Schmidlin and Wettstein for hecogenin derivatives,[2] and shown in the partial formulæ.

Connected with this work is an investigation of the possibility of introducing the 17α-hydroxy-group into 3β-hydroxy*allo*pregnane-12 : 20-dione, by the method of Julian *et al.*[7], with the sequence: 16 : 17-epoxide, 16-bromo-17α-hydroxy-compound, 17α-hydroxy-compound. In the last stage a difficulty was encountered: treatment of the bromohydrin with zinc and acetic acid yielded 3β-acetoxy*allo*pregnane-12 : 20-dione,

[5] Klyne, "Ciba Foundation Colloquia on Endocrinology," London, Churchill, 1953, Vol. 7, p. 127.
[6] Adams, Kirk, Patel, Petrow, and Stuart-Webb, *J.*, 1954, 2209, 2298.
[7] Julian, Meyer, Karpel, and Waller, *J. Amer. Chem. Soc.*, 1950, **72**, 5145.

perhaps by initial elimination of hypobromous acid to give the Δ^{16}-compound (cf. Fieser and Ettorre [8]) and reduction of the latter. The required 17α-hydroxy-20-ketone was obtained by debrominating the bromohydrin with Raney nickel in alcohol. Independently Mueller, Stobaugh, and Winniford [9] described this series of reactions but claimed to have obtained the 17α-hydroxy-compound with zinc and acetic acid. However, Dr. Mueller, in a personal communication, withdrew this claim: he had, in fact, obtained 3β-acetoxy-*allo*pregnane-12 : 20-dione. Adams *et al.*[6] obtained, as we did, the 17α-hydroxy-compound with Raney nickel and the 12 : 20-diketone with zinc. Before the work of Adams *et al.*[6] was published we had, independently, prepared, *via* the 21-bromo-derivative, 21-acetoxy-17α-hydroxy*allo*pregnane-3 : 12 : 20-trione; we wish only to place on record that our results are in complete accord with theirs.

Infrared absorption of the 12 : 20-dioxo-compounds examined showed certain anomalies in the solid state, particularly in the C=O stretching region, which tended to be more complex than was expected, an effect which may be attributed to some peculiarity of arrangement in the crystal.

Experimental

M. p.s were determined in a Kofler apparatus with polarised light, and are corrected. Optical rotations were determined in chloroform solutions of concentrations within the limits 0·5—1·0%. Infrared absorption was measured with a double-beam instrument with a rock-salt prism (Perkin-Elmer Model 21), KBr or KCl discs being used unless otherwise stated.

Reduction of 3β-*Acetoxy*allo*pregn*-16-*ene*-12 : 20-*dione*.—(*a*) Hydrogenation in the presence of 2% palladium–strontium carbonate gave 3β-acetoxy*allo*pregnane-12 : 20-dione, m. p. 197—199°, $[\alpha]_D^{21}$ +140° (cf. Mueller *et al.*[9] who give m. p. 189—190°). The same compound was obtained by using platinum in ethyl acetate or ethanol, or nickel in ethanol–ether, or by boiling an acetic acid solution with zinc powder. Boiling with 1% methanolic potassium hydroxide yielded 3β-*hydroxy*allo*pregnane*-12 : 20-*dione*, m. p. 189—195° (from acetone), $[\alpha]_D$ +165° (Found: C, 76·1; H, 9·5. $C_{21}H_{32}O_3$ requires C, 76·0; H, 9·7%). The infrared absorption in potassium chloride showed $\nu_{max.}$ 3420 (hydroxyl) and a triple peak, 1712, 1700, 1685 cm.$^{-1}$ in the C=O stretching region. A Nujol mull showed peaks at 1714, 1698, and 1682 cm.$^{-1}$ (calcium fluoride prism). A chloroformic solution showed a simple peak at 1708 cm.$^{-1}$.

(*b*) Hydrogenation of the acetoxypregnenedione (1 g.) in acetic acid (100 ml.), Adams's catalyst (50 mg.) being used, yielded a crude *acetate*, m. p. 148·5—152°, $[\alpha]_D^{21}$ −6° [infrared absorption in Nujol at about 3300 (hydroxyl), 1730 (acetate), and 1250 cm.$^{-1}$ (broad; acetate)], hydrolysed by 10% methanolic potassium hydroxide to allo*pregnane*-3β : 12ξ : 20β-*triol*, m. p. 230—234° (from ethyl acetate), $[\alpha]_D^{19}$ −2° (Found: C, 75·2; H, 10·7. $C_{21}H_{36}O_3$ requires C, 75·0; H, 10·8%), $\nu_{max.}$ (in Nujol) at approx. 3300 and a particularly intense, sharp peak at 1054 cm.$^{-1}$.

Bromination of 3β-*Acetoxy*allo*pregnane*-12 : 20-*dione*.—An ice-cold solution of the acetate (1 g.) in alcohol-free chloroform (20 ml.) was treated with bromine (0·16 ml., 1·1 equiv.) in chloroform (22 ml.). Ethanol was added and the solution kept overnight. The colourless solution was poured into water (100 ml.) containing sodium metabisulphite (0·25 g.). The chloroform layer was washed, dried, and evaporated, and the gum treated with methanol to give crystals, m. p. 167·5—171° (Found: C, 60·5; H, 8·0; Br, 17·9. $C_{23}H_{33}O_4Br$ requires C, 60·9; H, 7·3; Br, 17·7%), $\nu_{max.}$ (Nujol) 1720, 1713, and 1695 cm.$^{-1}$. A similar *product* was obtained by bromination in acetic acid solution. The product was dehydrobrominated by boiling collidine and, after purification by chromatography, rather poorly crystalline material was isolated, identified by its infrared absorption as 3β-acetoxy*allo*pregn-16-ene-12 : 20-dione. When 2·2 or 3·3 equivalents of bromine were used in the bromination another *product* was obtained, approximating to a tribromide, m. p. 195—197° (decomp.) or 198—200° (decomp.) (from alcohol), $[\alpha]_D$ −55° (Found: C, 45·6; H, 5·4; Br, 39·0. $C_{23}H_{31}O_4Br_3$ requires C, 45·2; H, 5·1; Br, 39·3%), $\nu_{max.}$ (Nujol) 1720 and 1693 cm.$^{-1}$.

12 : 12-*Ethylenedioxy*-3β-*hydroxy*allo*pregnane*-12 : 20-*dione*.—A solution was prepared by boiling under reflux with a Dean and Stark water trap, and in a current of nitrogen, a mixture of toluene (100 ml.), freshly distilled ethylene glycol (3 ml.), and toluene-*p*-sulphonic acid (50 mg.). When the condensate had become clear, 3β-acetoxy*allo*pregnane-12 : 20-dione (1·8 g.) was added

[8] Fieser and Ettorre, *J. Amer. Chem. Soc.*, 1953, **75**, 1700.
[9] Mueller, Stobaugh, and Winniford, *ibid.*, p. 4888.

and boiling continued until no more water condensed (2 hr.). The cooled solution was washed with sodium hydrogen carbonate solution and water, dried, and evaporated under reduced pressure. The residue with methanol yielded the *ketal acetate* (1·27 g.), m. p. 157—160°, rising to 161—164·5° on recrystallisation, $[\alpha]_D^{22}$ +104° (Found, after drying at 90° *in vacuo*: C, 71·7; H, 9·2. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·2%), $\nu_{max.}$ 1725 and 1700 and ($CHCl_3$) 1720 and inflexion at 1705 cm.$^{-1}$. Hydrolysis of the acetate by 5% methanolic sodium hydroxide at room temperature and crystallisation of the product from ethyl acetate–light petroleum (b. p. 60—80°) gave 12 : 12-*ethylenedioxy*-3β-*hydroxy*allo*pregnane*-12 : 20-*dione*, m. p. 198·5—200°, $[\alpha]_D^{21}$ +115° (Found: C, 73·1; H, 9·6. $C_{23}H_{35}O_4$ requires C, 73·3; H, 9·65%), $\nu_{max.}$ 1702 cm.$^{-1}$ in potassium bromide; a single peak was also observed in carbon disulphide. Resolution into two adjacent peaks was observed in a Nujol mull.

Bromination of 3β-hydroxy*allo*pregnane-12 : 20-dione and the 12-ethylene ketal was carried out under the same conditions for each substance, in ice-cold chloroform with 1·1 equiv. of bromine. The products, crystallised from benzene–light petroleum (b. p. 60—80°), had m. p. 131—134° and 133—135°, respectively. They had identical infrared absorptions with $\nu_{max.}$ (CS_2) 1715 and 1700 cm.$^{-1}$ or (Nujol) 1695 cm.$^{-1}$. The composition approximated to that of a monobromo*allo*pregnane-12 : 20-dione (Found, for the product from the ketal: C, 58·8; H, 7·5; Br, 23·4. Calc. for $C_{21}H_{31}O_3Br$: C, 61·4; H, 7·6; Br, 19·5%).

Reduction of the 12-Ethylene Ketal or its Acetate.—(a) *Wolff–Kishner method.* The ketal (2·47 g.), treated with sodium methoxide [from sodium (3 g.) and methanol (34 ml.)] and hydrazine hydrate (95%; 3·3 ml.) at 200° for 6 hr. yielded material which was purified by adsorption from benzene solution on alumina and elution with benzene containing 10% of chloroform. The product, 3β-*hydroxy*allo*pregnan*-12-*one* (1 g.), had m. p. 197—199° (from hexane), $[\alpha]_D^{21}$ +109° (Found: C, 79·5; H, 11·1. $C_{21}H_{34}O_2$ requires C, 79·2; H, 10·8%). The infrared absorption spectrum showed bands at 3220 (hydroxyl) and 1698 (ketone) and an intense sharp peak at 1040 cm.$^{-1}$. The *acetate*, crystallised from aqueous methanol, had m. p. 138—141·5°, $[\alpha]_D^{21}$ +86° (Found: C, 76·5; H, 10·3. $C_{23}H_{36}O_3$ requires C, 76·6; H, 10·1%), $\nu_{max.}$ 1725 (acetate), 1700 (ketone), and 1247 cm.$^{-1}$ (acetate).

(b) *With lithium aluminium hydride.* A solution of 3β-acetoxy-12 : 12-ethylenedioxy*allo*pregnan-20-one (3·3 g.) in dry ether (150 ml.) was added dropwise to a suspension of lithium aluminium hydride (1 g.) in ether (150 ml.). The reaction was completed by boiling (1 hr.). After dilution with water the ethereal solution and extract were washed, dried, and evaporated. The residue (2·8 g.) yielded 12 : 12-*ethylenedioxy*allo*pregnane*-3β : 20β-*diol* in prisms (from acetone), m. p. 197—202°, $[\alpha]_D^{21}$ +48° (Found: C, 73·1; H, 10·2. $C_{23}H_{38}O_4$ requires C, 73·0; H, 10·1%). There was intense absorption in the infrared at 3400 cm.$^{-1}$ (hydroxyl), but none in the C=O stretching region. By boiling the ketal-diol with methanolic hydrochloric acid 3β : 20β-*dihydroxy*allo*pregnan*-12-*one* was obtained, m. p. 238—243°, $[\alpha]_D^{21}$ +91° (Found: C, 75·3; H, 10·2. $C_{21}H_{34}O_3$ requires C, 75·3; H, 10·3%), $\nu_{max.}$ 3440 (shoulder at 3380) (hydroxyl) and 1680 cm.$^{-1}$ (ketone). The 3β-*monoacetate*, obtained by heating with acetic anhydride for 1 hr. at 100°, had m. p. 199—207°, $[\alpha]_D^{21}$ +72°, $\nu_{max.}$ 3400 (sharp: hydroxyl), 1738 (acetate), 1685 (ketone), and 1245 cm. (acetate). When acetylation was carried out in boiling acetic anhydride for 1 hr. the product was the *diacetate*, crystals (from acetone or hexane), m. p. 141—143°, $[\alpha]_D^{21}$ +96° (Found: C, 71·4; H, 9·0. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·2%). The infrared absorption showed no hydroxyl band, but there was a broad, unresolved band, $\nu_{max.}$ at 1725 cm.$^{-1}$ in the C=O stretching region, and a band at 1245 cm.$^{-1}$ (acetate).

11α-*Bromo*-3β : 20β-*dihydroxy*allo*pregnan*-12-*one*.—The diacetate (0·75 g.) in benzene (10 ml.) was treated with bromine (1·1 equiv.) in benzene (2·5 ml.). After 15 min. the bromine was completely absorbed and a precipitate was formed which dissolved after stirring for a further 30 min. The washed, dried benzene solution was evaporated at 35° under reduced pressure. The residue gave, from hexane, 3β : 20β-*diacetoxy*-11α-*bromo*allo*pregnan*-12-*one* (0·5 g.), m. p. 161—178°, $[\alpha]_D^{21}$ +56° (Found: C, 60·3; H, 7·6; Br, 15·3. $C_{25}H_{37}O_5Br$ requires C, 60·3; H, 7·5; Br, 16·1%), $\nu_{max.}$ 1730 (acetate and, presumably, ketone) and 1250 cm.$^{-1}$ (acetate).

Reduction of 3β : 20β-*Diacetoxy*-11α-*bromo*allo*pregnan*-12-*one*.—Saturated aqueous sodium hydrogen carbonate solution (5 ml.) was added to a solution of the bromo-ketone (5·14 g.) in ethanol (175 ml.) and dioxan (20 ml.). The turbid mixture was treated with sodium borohydride (0·7 g.) and stirred for 2½ hr. at 35°, and water was then added. An ethereal extract was washed, dried, and evaporated, yielding an oily residue (5·2 g.). A portion (2·4 g.) of this, dissolved in light petroleum (b. p. 60—80°), was chromatographed on neutral alumina (75 g.); the following fractions were eluted: benzene–light petroleum (1 : 40) gave successively (*a*) 0·07 g. and (*b*) 0·42 g. The proportion of benzene was increased, finally reaching 100%, and the

eluates (*c*) 1·31 g. and (*d*) 0·07 g. were obtained. Ether–benzene (1 : 1) eluted (*e*) 0·2 g. Fraction (*a*) yielded from hexane 11β : 12β-*epoxy*allo*pregnane*-3β : 20β-*diol diacetate*, m. p. 153—155°, $[\alpha]_D^{23}$ +51° (Found : C, 72·1; H, 9·2. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·2%), $\nu_{max.}$ 1730 and 1240 (acetate), 868 cm.$^{-1}$ (epoxide), and a prominent band at 1025 cm.$^{-1}$. There was no significant absorption due to a hydroxyl group. Hydrolysis with methanolic potassium hydroxide gave 11β : 12β-*epoxy*allo*pregnane*-3β : 20β-*diol*, m. p. 216—226°, $[\alpha]_D^{22}$ +5° (Found : C, 75·6; H, 10·1. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·2%), $\nu_{max.}$ 3400 (hydroxyl), 1034 (C–O), and 860 cm.$^{-1}$ (epoxide). Fraction (*b*) yielded, from hexane, 11α-*bromo*allo*pregnane*-3β : 12β : 20β-*triol* 3 : 20-*diacetate*, m. p. 170—172·5°, $[\alpha]_D^{21}$ +10° (Found : C, 60·0; H, 7·8; Br, 16·3. $C_{25}H_{39}O_5Br$ requires C, 60·1; H, 7·9; Br, 16·0%), $\nu_{max.}$ 3540 (hydroxyl), 1730 and 1245 (acetate), 1025 cm.$^{-1}$ (C–O). When boiled with 3% methanolic potassium hydroxide this was converted into 11β : 12β-epoxy*allo*pregnane-3β : 20β-diol, identical with the compound from fraction (*d*). Fraction (*c*), crystallised from hexane, yielded 11α-*bromo*allo*pregnane*-3β : 12α : 20β-*triol* 3 : 20-*diacetate*, m. p. 160—164°, $[\alpha]_D^{21}$ +5° (Found : C, 60·15; H, 7·8; Br, 16·5. $C_{25}H_{39}O_5Br$ requires C, 60·1; H, 7·9; Br, 16·0%). The infrared absorption was similar to that of the 12β-hydroxy-compound, but the hydroxyl peak was much blunter, and there were differences in the 1100—1000 cm.$^{-1}$ range. Hydrolysis by 1% methanolic potassium hydroxide yielded 3β : 20β-dihydroxy*allo*pregnan-12-one, m. p. 238—241·5°, identical with the material already described above.

Fraction (*d*) gave, from acetone–hexane, 11β-*bromo*allo*pregnane*-3β : 12α : 20β-*triol* 3 : 20-*diacetate*, m. p. 214—221°, $[\alpha]_D^{25}$ +49°. Hydrolysis by alkali yielded the (?)11α : 12α-epoxide, m. p. 200—220°, $\nu_{max.}$ 3400 (hydroxyl) and 866 cm.$^{-1}$ (epoxide) with no absorption in the C=O stretching region; an intense sharp peak was present at 1033 cm.$^{-1}$ (C–O). Fraction (*e*) gave, from acetone–hexane, (?)11β-*bromo*allo*pregnane*-3β : 12α : 20β-*triol* 3-*acetate*, m. p. 210—217°, $[\alpha]_D^{23}$ −20° (Found : C, 60·6; H, 8·0; Br, 17·6. $C_{23}H_{37}O_4Br$ requires C, 60·3; H, 8·15; Br, 17·5%), $\nu_{max.}$ 3430, 3280 (hydroxyl), 1725, 1703 (s) (? acetate), 1270, 1255 cm.$^{-1}$ (acetate). From the fact that on hydrolysis with methanolic potassium hydroxide it gave the same (?)11α : 12α-epoxide as the diacetate from fraction (*d*) it seems likely that the compound has the constitution allotted to it, but the lævorotation is anomalous. The compounds in fractions (*d*) and (*e*) presumably arise from 11β-bromo-ketone contaminating the 11α-bromo-compound.

allo*Pregnane*-3 : 11 : 20-*trione*.—(*a*) The 11β : 12β-epoxide (70 mg.) obtained from fractions (*a*) and (*b*) by hydrolysis was shaken in chloroform (10 ml.) with 48% hydrobromic acid (0·5 ml.). After 30 min. the chloroform was washed with water and evaporated. The residue, crystallised from acetone–hexane, yielded 12α-bromo*allo*pregnane-3β : 11β : 20β-triol (68 mg.), m. p. 204—210°, $[\alpha]_D^{23}$ +17° (dioxan), $\nu_{max.}$ 3380 cm.$^{-1}$ (hydroxyl). The triol (66 mg.) in acetic acid (4 ml.) was treated with chromic oxide (0·1 g.) in water (1 ml.), the mixture was shaken well and after 1½ hr. the product was extracted into chloroform and the extract was washed, dried, and evaporated. The bromo-ketone, m. p. 176—179° (from acetone–hexane), $\nu_{max.}$ 1700 (s), was debrominated by boiling with zinc in acetic acid solution. *allo*Pregnane-3 : 11 : 20-trione, m. p. 112—118°, was isolated, identical with an authentic specimen and with the material described below.

(*b*) An alternative preparation of the triketone began with the 11β : 11β-epoxy*allo*pregnane-3β : 20β-diol diacetate from fraction (*a*) of the chromatographic separation. This material (60 mg.) in chloroform (3 ml.) was treated with 48% hydrobromic acid (0·3 ml.). After 30 min. the solution was washed free from acid and evaporated, and the 12α-bromo*allo*pregnane-3β : 11β : 20β-triol 3 : 20-diacetate crystallised from acetone–hexane.

The triol diacetate (70 mg.) in 80% acetic acid (5 ml.) was treated with chromic oxide (70 mg.). After 1½ hr. water was added and the product was isolated with chloroform. 3β : 20β-Diacetoxy-12α-bromo*allo*pregnan-11-one crytallised from acetone–hexane. Debromination by zinc dust in acetic acid yielded 3β : 20β-diacetoxy*allo*pregnan-11-one (from ether–pentane), m. p. 165—173°, $[\alpha]_D^{22}$ +34°, $\nu_{max.}$ 1730 (strong; acetate), 1705 (lower; ketone), 1245 cm.$^{-1}$ (acetate). This material was hydrolysed with 10% methanolic potassium hydroxide, and the crude product oxidised with chromic oxide in acetic acid. The final product was *allo*pregnane-3 : 11 : 20-trione (from acetone–hexane), m. p. 212—218° (Found : C, 75·9; H, 8·9. Calc. for $C_{21}H_{30}O_3$: C, 76·3; H, 9·15%). The infrared absorption, with a strong band at 1705 cm.$^{-1}$, was completely identical throughout the whole spectrum with that of an authentic specimen of the trione, m. p. 211—220° (Steiger and Reichstein [10] gave m. p. 212—216°).

Rockogenin (12β-*Hydroxytigogenin*).—Hecogenin acetate was reduced by sodium borohydride, and the product purified as the acetate which, crystallised twice from methanol

[10] Steiger and Reichstein, *Helv. Chim. Acta*, 1938, **21**, 161.

(charcoal), had m. p. 199—207°, $[\alpha]_D^{22}$ −60° (dioxan). Alkaline hydrolysis yielded rockogenin (from methanol), m. p. 195—200°, $[\alpha]_D^{22}$ −63° (dioxan) {(Hirschmann *et al.*[11] give 218·5—220·5°, $[\alpha]_D$ −64° (acetone)}.

3β : 12β-*Diacetoxy*allo*pregn*-16-*en*-20-*one* was obtained by conversion of rockogenin into ψ-rockogenin by the method of Cameron *et al.*[12], acetylation of the crude product, oxidation of the acetate with chromic acid in 90% acetic acid, hydrolysis of the "diosone," and reacetylation. The product crystallised from 50% aqueous methanol and had m. p. 140—143°, $[\alpha]_D^{22}$ +19° (Found: C, 72·0; H, 8·6. $C_{25}H_{36}O_5$ requires C, 72·0; H, 8·8%), $\nu_{max.}$ 1735 (acetate), 1680 (ketone), 1590 (double bond), 1250 cm.$^{-1}$ (acetate).

3β : 12β-*Diacetoxy*allo*pregnan*-20-*one*.—The Δ^{16}-compound was hydrogenated in ethyl acetate solution, 2% palladium–strontium carbonate being used as catalyst. The gum after purification by chromatography on alumina, was crystallised from pentane and from aqueous methanol, yielding 3β : 12β-*diacetoxy*allo*pregnan*-20-*one*, m. p. 109—113°, $[\alpha]_D^{19}$ +48° (Found: C, 71·7; H, 9·3. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·2%), $\nu_{max.}$ 1735 (strong; acetate), 1710 (lower; ketone), 1250 cm.$^{-1}$ (acetate). There were many minor, but quite distinctive, differences in the "fingerprint" region from the absorption spectrum of the isomeric 3β : 20β-diacetoxy*allo*-pregnan-12-one.

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