Formation of Some Novel 9β-Methyl-19-norpregnane Derivatives

By **Alex C. Campbell,* Colin L. Hewett, Maurice S. Maidment,** and **Gilbert F. Woods,** Organon Scientific Development Group, Newhouse, Lanarkshire ML1 5SH, Scotland

The rearrangement of 9α,11α-epoxy-5α-pregnane-3β-20β-diyl diacetate (3) to 11-oxo-5α,9β-pregnane-3β,20β-diyl diacetate (4) and 11α-hydroxy-9β-methyl-19-norpregn-5(10)-ene-3β,20β-diyl diacetate (5) is reported. Treatment of the 5(10)-ene (5) with *m*-chloroperbenzoic acid in benzene affords 5β,10β-epoxy-11α-hydroxy-9β-methyl-19-norpregnane-3β,20β-diyl diacetate (11), whereas epoxidation with peracetic acid in acetic acid containing mineral acid (1% H_2SO_4) leads to 5α,11α-epoxy-10β-hydroxy-9β-methyl-19-norpregnane-3β,20β-diyl diacetate (12) by rearrangement of the initially formed 5β,10β-epoxide (11).

INVERSION of the configuration at an angular position in the steroid skeleton significantly alters the conformation, a pronounced change attending inversion at C-8 and C-9. In an attempt to prepare, by partial backbone rearrangement, novel steroids having unusual conformations, the epoxy-diacetate (3) was treated with boron trifluoride–ether complex; the results are now described.

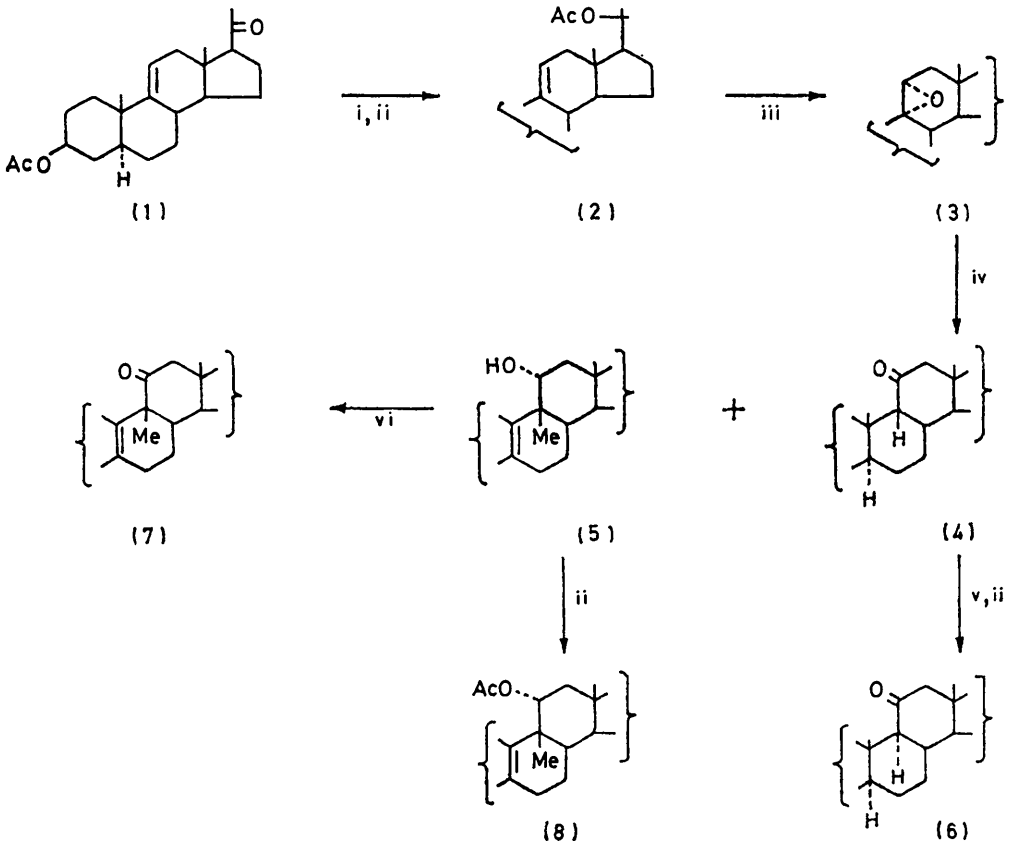
The known diacetate (2),[1] obtained from the readily available keto-acetate (1) [2] by reduction with sodium borohydride and acetylation, was converted with peracetic acid into the expected epoxy-diacetate (3) in high yield. The α-configuration for the epoxy-function was confirmed by the n.m.r. shifts exhibited by the C-18 and C-19 protons (0·06 and 0·16 p.p.m., respectively) which

[1] C. Amiard, R. Heymes, T. van Thuong, and J. Mathieu, *Bull. Soc. chim. France*, 1965, 2321.

[2] C. Djerassi, H. Martinez, and G. Rosenkranz, *J. Org. Chem.*, 1951, 1278.

attended conversion of the $\Delta^{9(11)}$-compound (2) into the epoxide (3). The shifts were in accord with the Zurcher values.[3]

Treatment of a solution of (3) in ether with boron trifluoride afforded essentially a two-component mixture (*ca.* 1 : 1 by g.l.c.) which was resolved by gradient elution chromatography on silica gel. The less polar product, 11-oxo-5α,9β-pregnane-3β,20β-diyl diacetate (4), was isolated in a pure state in 35% yield and identified from spectroscopic data and its conversion into the known 9α-epimer (6)[4] on treatment with 10% potassium hydroxide in boiling ethanol and subsequent acetylation. *m/e* 358·2510 (loss of acetic acid from $C_{25}H_{38}O_5$). The tetranitromethane test established the presence of a double bond, and the absence of strong u.v. absorption above 212 nm established that this is not conjugated. The i.r. spectrum showed hydroxy- and carbonyl absorption. The n.m.r. spectrum exhibited signals for two tertiary methyl groups, a secondary methyl group, two acetoxy-groups, and one carbinol proton, which appeared as a double doublet at δ 3·65 (*J* 12 and 4 Hz). The hydroxy-group is thus secondary and the absence of signals for olefinic protons showed that the double bond is tetrasubstituted. The ready conversions of the



Reagents: i, $NaBH_4$; ii, Ac_2O–C_5H_5N; iii, AcO_2H–AcOH; iv, BF_3,Et_2O–Et_2O; v, KOH–EtOH; vi, H_2CrO_4–Me_2CO

The low-field n.m.r. doublet (δ 2·81, *J* 9 Hz) for the 9β-proton in the ketone (4) is in accord with earlier reports.[5]

Rearrangement of the epoxide (3) to the ketone (4) probably proceeds *via* attack on the epoxy-function by boron trifluoride with a concomitant 1,2-shift of the 11β-proton to the 9β-position.[6]

The more polar product, isolated in a pure state in 21% yield, is formulated as 11α-hydroxy-9β-methyl-19-norpregn-5(10)-ene-3β,20β-diyl diacetate (5) on the following evidence. The compound showed a parent ion at

[3] N. S. Bhacca and D. H. Williams, 'Application of NMR spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 13.

[4] J. Romo, G. Stork, G. Rosenkranz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 2918.

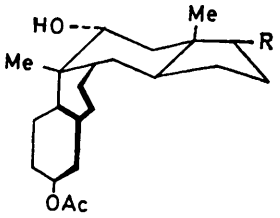
alcohol (5) into a ketone (7) and a triacetate (8) confirmed that the hydroxy-group is secondary.

Confirmation that the hydroxy-group in (5) is at C-11 was obtained from the n.m.r. spectrum of the ketone (7), which displayed an AB quartet for the C-12 methylene protons at δ 2·26 and 2·40 (*J* 12·5 Hz), and assignment of the α-configuration to the hydroxy-group followed from the mode of the backbone rearrangement of the epoxide (3). Moreover, models indicate that the alcohol (5) probably exists in the conformation (A), which is apparently the least strained. Hence the coupling

[5] G. F. H. Green, J. E. Page, and S. E. Staniforth, *J. Chem. Soc.*, 1965, 7328.

[6] P. Bladon, H. B. Henbest, E. R. H. Jones, B. J. Lovell, G. W. Wood, G. F. Woods, J. Elks, R. M. Evans, D. E. Hathaway, J. F. Oughton, and G. H. Thomas, *J. Chem. Soc.*, 1953, 2921.

constants and multiplicity of the 11β-proton signal agree with its axial configuration and the presence of a substituent at C-9.

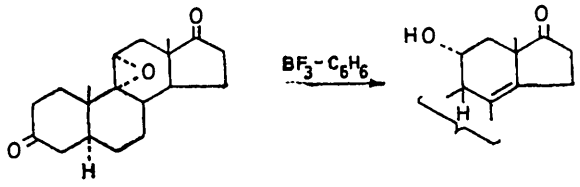


(A) $\Delta^{5(10)}$

(A') $\Delta^{1,3,5(10)}$

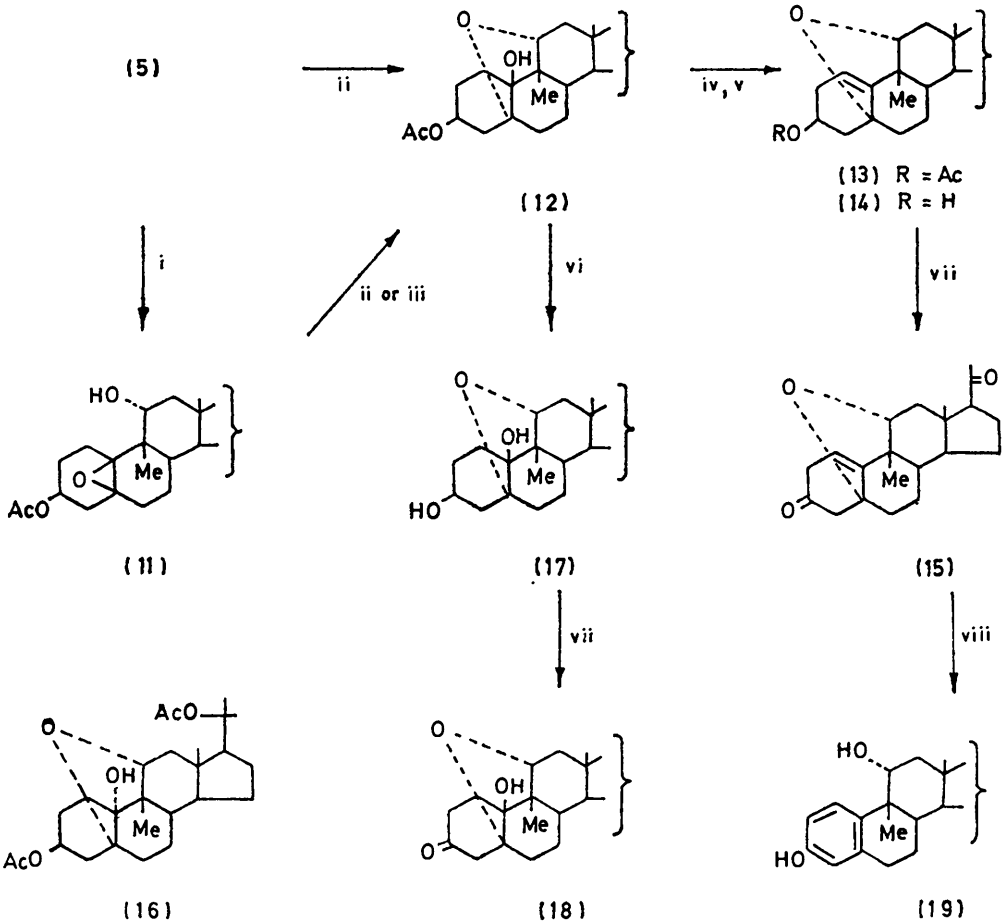
The structure of the backbone rearrangement product (5) was confirmed by a comparison of the derived 11-ketone (7) with an authentic sample [7] {Dr. Edwards has informed us that the chemical shift reported by him for the C-9 methyl group [δ ($CDCl_3$) 1·32] is in error and that his value is in agreement with ours [δ ($CDCl_3$) 1·18]}.

A surprising feature of the reaction was the absence of detectable amounts of product arising from 1,2-hydride shifts involving C-8 and C-14 protons, since ApSimon [8] has reported that the major product obtained by treatment of 9α,11α-epoxy-5α-androstane-3,17-dione (9) with boron trifluoride gas in benzene is the hydroxy-dione (10). This difference was not due to a difference in conditions, since on treating the epoxide (3) under those employed by ApSimon we obtained essentially the same mixture that resulted from the rearrangement of (3) with boron trifluoride in ether.



(9) (10)

Molecular models indicate that whereas in the alcohol (5) all the rings can adopt chair or half-chair conformations, ring B in the alcohol (10) must necessarily be in a boat or deformed boat conformation. Therefore it is



Reagents: i, *m*-$ClC_6H_4{\cdot}CO_3H$–C_6H_6; ii, AcO_2H–AcOH–H_2SO_4; iii, AcOH–H_2SO_4; iv, $SOCl_2$–C_5H_5N; v, KOH–MeOH; vi, K_2CO_3–EtOH; vii, H_2CrO_4–Me_2CO; viii, KOH–EtOH

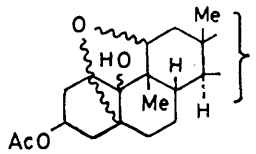
[7] O. E. Edwards and T. Sano, *Canad. J. Chem.*, 1969, **47**, 3489.
[8] J. W. ApSimon, R. R. King, and J. J. Rosenfeld, *Canad. J. Chem.*, 1969, **47**, 1989.

likely that, in the absence of other over-riding factors [*e.g.* the strongly electron-withdrawing carbonyl–boron trifluoride complex system at C-3 such as would result on treatment of (9) with boron trifluoride], the preferred rearrangement of 9α,11α-epoxides in the 5α-series involves a methyl shift from C-10 to C-9.

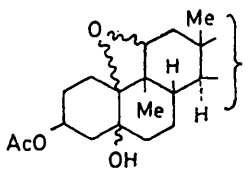
The $\Delta^{5(10)}$-diacetate (5) reacted with *m*-chloroperbenzoic acid in benzene to give the 5β,10β-epoxide (11) as the major product (>90% by g.l.c.). Treatment of (5) with peracetic acid in acetic acid containing a small amount of sulphuric acid (0·15%) for 7 days furnished the 5α,11α-epoxide (12) in high yield. When the reaction was carried out using a higher concentration of sulphuric acid (0·3%) it was complete in 18 h. By following the reaction by g.l.c. it was shown that the 5α,11α-epoxide was an acid-catalysed rearrangement product of the initially formed 5β,10β-epoxide (11), the production of which was the rate limiting step. This was confirmed by the nearly quantitative conversion of the 5β,11β-epoxide (11) into the 5α,11α-epoxide (12) in 18 h by acetic acid containing sulphuric acid (0·15%), either alone or with peracetic acid.

The 5β,10β-epoxide (11) was not converted into the 5α,11α-epoxide (12) by either acetic acid alone or peracetic acid in acetic acid buffered with sodium acetate.

The configurations of the two isomeric epoxides (11) and (12) were deduced as follows. For the epoxide (12), no strong u.v. absorption was observed, and the i.r. spectrum revealed the presence of a hydroxy-group, shown to be tertiary by its resistance to acetylation and oxidation. The n.m.r. spectrum exhibited signals for two acetoxy-groups, two angular methyl groups, and a secondary methyl group, and a doublet at δ 3·85 (1H, *J* 6 Hz). The data were thus consistent with one of the partial structures (B) and (C).



(B)



(C)

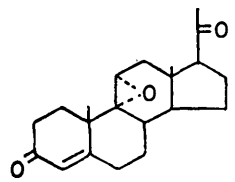
The location of the hydroxy-group at C-10 was established by dehydration of (12) with thionyl chloride–pyridine, which afforded the $\Delta^{1(10)}$-diacetate (13) as the only product. The location of the double bond of this diacetate was confirmed by the following evidence. Basic hydrolysis of the diacetate (13) furnished the diol (14), which was oxidised with Jones reagent to the diketone (15), the n.m.r. spectrum of which displayed an ABX system. The X part was a pseudo-triplet at δ 5·5 (1H, $J_{AX,BX}$ 3·5 Hz, 1-H) and the AB part consisted of eight lines centred at δ 2·84 (2H, J_{AB} 22, $J_{AX,BX}$ 3·5 Hz, 2-H_2). The eight-line pattern collapsed to an AB quartet on irradiation at the frequency of the pseudo-triplet, and irradiation at the centre of the AB part of the ABX system caused the triplet to collapse to a singlet. These data firmly established structure (15) for the oxidation product, and are inconsistent with both the Δ^4- and the Δ^5-dione structures, which could result from dehydration and oxidation if the precursor contained a 5-hydroxy group [partial structure (C)].

The configurations of the hydroxy- and epoxy-groups in (12) were deduced as follows. Molecular models show that only two isomers having the partial structure (B) are possible, namely the 10β-hydroxy-5α,11α-epoxide (12) and its 10α-epimer (16). Models also reveal that the 3β-acetoxy-group in (16) is axial whereas in (12), it is equatorial and therefore more susceptible to hydrolysis. The C-10 hydroxy-group is assigned the β-configuration because treatment of the diacetate (12) with potassium carbonate in boiling methanol for 30 min afforded in nearly quantitative yield the 20β-monoacetate (17). That the 3-acetoxy-group had been selectively hydrolysed was established by the appearance of a doublet in the n.m.r. spectrum for the C-21 protons attending the conversion of the diol (17) into the ketone (18).

Additional support for the identification of the 10-hydroxy-5,11-epoxide as (12) and not the 10α-epimer (16) was obtained from c.d. measurements on the derived ketone (18), which displayed a positive curve ([θ] +1250; $\lambda_{max.}$ 294 nm). Molecular models indicate that a positive c.d. curve would be as expected for (18), whereas the curve of its 10α-epimer would be expected to be negative.

The epoxy-group in (11) is assigned the β-configuration because attack with mineral acid resulted in the formation of the 10β-hydroxy-5α,11α-epoxide (12), *i.e.* the product from normal *trans*-cleavage of the 5β,10β-epoxide group. Moreover, attack by the epoxidising agent on the hydroxy-olefin (5) would take place on the β-face of its cage-like structure (A).

Treatment of the diketone (15) with potassium hydroxide in ethanol afforded a high yield of the 9β-methyl ring-A-aromatic derivative (19). ApSimon and his collaborators [8] claim to have isolated this product in 2% yield after treatment of the αβ-unsaturated ketone (20) with boron trifluoride in benzene. The constants and spectroscopic data reported for their compound however are not consistent with ours. We consider that the structure of the $\Delta^{1(10)}$-5α,11α-epoxide (13) has been



(20)

rigorously established, and, except for the configuration at C-17, the identification of our samples of the ring-A-aromatic steroid (19) and the intermediates [diol (14) and dione (15)] is supported by substantial spectroscopic evidence.

The 17-acetyl group in (19) is designated as β on the basis of the following argument. It has been shown that hydrolysis of the diacetate (13) and subsequent oxidation with Jones reagent gives an almost quantitative yield of crude diketone (15) (n.m.r.). Similarly, the almost instantaneous rearrangement of the diketone (15) to the ring-A-aromatic compound (19) with dilute ethanolic potassium hydroxide was also almost quantitative. Hence, the oxidation and aromatisation was accompanied either by complete or by no epimerisation of the 17-acetyl group. Complete epimerisation under these conditions is regarded as unlikely. Furthermore, since the ketone (19) probably has the conformation (A'), the 17β-acetyl epimer is presumably the thermodynamically stable one.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. Unless otherwise stated, u.v. spectra were measured for solutions in ethanol with a Perkin-Elmer 402 spectrophotometer, i.r. spectra for solutions in methylene chloride with a Perkin-Elmer 457 spectrophotometer, and n.m.r. spectra for solutions in [^{2}H]chloroform with a Varian A60. Mass spectra were measured with an A.E.I. MS-9 instrument. Specific rotations were determined for solutions in chloroform unless indicated to the contrary. G.l.c. analyses were performed on a 3% SE 30 column at 227°.

Concentrations (*c*) are quoted in g per 100 ml.

5α-*Pregn*-9(11)-*ene*-3β,20β-*diyl Diacetate* (2).—A solution of 20-oxo-5α-pregn-9(11)-en-3β-yl acetate (1) (84 g) in tetrahydrofuran (315 ml) and methanol (480 ml) was treated with sodium borohydride (21 g) in portions with stirring at room temperature for 1 h. The solution was neutralised with acetic acid and poured into water (7 l) at 0°. The precipitate was filtered off, washed with water, and dried under reduced pressure, and the crude product (83·5 g) was acetylated with acetic anhydride–pyridine. Isolation with ether yielded the diacetate (2) (74 g) as stout needles, m.p. 121—123° (from methanol), $[\alpha]_D$ +22° (*c* 0·6) (lit.,[1] m.p. 125°, $[\alpha]_D$ +20°); δ 0·57 and 0·94 (each 3H, s, 10- and 13-Me).

9α,11α-*Epoxy*-5α-*pregnane*-3β,20β-*diyl Diacetate* (3).—A solution (30%; 60 ml) of commercial peracetic acid in acetic acid was added to a solution of the diacetate (2) (72 g) in glacial acetic acid (1 l). The mixture was kept at room temperature overnight, then poured into water (7 l) at 0° containing sodium hydrogen sulphite (25 g). The precipitate was filtered off, washed with hot water, dried under reduced pressure, and recrystallised from methanol to yield the *epoxide* (3) (68 g) as platelets, m.p. 172—175°, $[\alpha]_D$ −6° (*c* 0·6); $\nu_{max.}$ 1722 cm^{-1} (OAc); δ 0·63 and 1·10 (each 3H, s, 10- and 13-Me), 1·13 (3H, d, *J* 5 Hz, 20-Me), 1·99 and 2·01 (each 3H, s, 3β- and 20β-OAc), 3·10 (1H, pseudo-t, *J* 3 Hz, 11β-H), and 4·75 (2H, m, $W_{\frac{1}{2}}$ 20 Hz, 3α-H and 20α-H) (Found: C, 71·9; H, 9·15. $C_{25}H_{38}O_5$ requires C, 71·75; H, 9·15%).

11-*Oxo*-5α,9β-*pregnane*-3β,20β-*diyl Diacetate* (4), *and* 11α-*Hydroxy*-9β-*methyl*-19-*norpregn*-5(10)-*ene*-3β,20β-*diyl Diacetate* (5).—*Method A*. Freshly distilled boron trifluoride–diethyl ether (21 ml) was added to a stirred solution of the epoxide (3) (21 g) in dry benzene (200 ml). The mixture was stirred for 70 h at room temperature in a sealed flask until all the starting material had reacted (g.l.c.), then diluted with ether and poured into aqueous 5% potassium hydrogen carbonate at 0°. Isolation in the usual manner and recrystallisation from acetone–hexane gave the *ketone* (4) (1·61 g) as needles, m.p. 171—174°, $[\alpha]_D$ +89° (*c* 1·0); $\nu_{max.}$ 1730 and 1725 (OAc), and 1710 [C(11)=O]; δ 0·92 and 1·08 (each 3H, s, 10- and 13-Me), 1·14 (3H, d, *J* 7 Hz, 20-Me), 1·99 (each 3H, s, 3β- and 20β-OAc), 2·27 (2H, s, 12-H$_2$), 2·81 (1H, d, *J* 9 Hz, 9β-H), and 4·5—5·2 (2H, m, 3α-H and 20α-H) (Found: C, 71·8; H, 9·05. $C_{25}H_{38}O_5$ requires C, 71·75; H, 9·15%). The mother-liquor from the crystallisation, which was essentially a two-component mixture (g.l.c.), was taken to dryness and the residue in benzene was chromatographed on silica (800 g) (gradient elution with dry benzene and dry acid-free ethyl acetate). The fractions containing the less polar component when crystallised from acetone–hexane afforded a further quantity (5·86 g) of the 11-ketone (4). The more polar component yielded the *hydroxy-diacetate* (5) (4·31 g) as needles, m.p. 172—175° (from acetone–hexane), $[\alpha]_D$ −53° (*c* 1·0); no strong u.v. absorption above 212 nm; $\nu_{max.}$ 3620 (OH) and 1725 cm^{-1} (OAc); δ 0·72 and 1·20 (each 3H, s, 9- and 13-Me), 2·01 (6H, s, 3β- and 20β-OAc), 3·65 (1H, dd, $J_{ax,ax}$ 12, $J_{ax,eq}$ 4 Hz, 11β-H), and 4·60—5·20 (2H, m, 3α-H and 20α-H). The tetranitromethane test gave a positive result [Found: C, 71·9; H, 9·4%; *m/e*, 358·2510. $C_{25}H_{38}O_5$ requires C, 71·75; H, 9·15%; $C_{23}H_{34}O_3$ (*M* − AcOH) requires *m/e*, 358·2509].

Method B. A solution of the epoxide (3) (100 mg) in dry benzene (20 ml) was treated with boron trifluoride gas according to the method described by ApSimon.[8] The product was a mixture similar to that obtained by method A (t.l.c., g.l.c.).

9β-*Methyl*-19-*norpregn*-5(10)-*ene*-3β,11α,20β-*triyl Triacetate* (8).—Prepared by acetylation of the alcohol (5), this *triacetate* gave needles, m.p. 148—153° (from acetone–hexane), $[\alpha]_D$ −64° (*c* 0·8); $\nu_{max.}$ 1742, 1730, and 1725 cm^{-1} (OAc); δ 0·79 and 1·07 (each 3H, s, 9- and 13-Me), 1·13 (3H, d, *J* 7·5 Hz, 20-Me), 1·97 and 2·03 (each 3H, s, 3β- and 20β-OAc), and 4·55—5·20 (2H, m, 3α-H and 20α-H) (Found: C, 70·1; H, 8·85. $C_{27}H_{40}O_6$ requires C, 70·4; H, 8·75%).

11-*Oxo*-5α-*pregnane*-3β,20β-*diyl Diacetate* (6).[4]—A solution of the ketone (4) (100 mg) in ethanol (10 ml) containing potassium hydroxide (1 g) was boiled for 16 h under nitrogen, concentrated under reduced pressure, and poured into water. The product was isolated with ether. Acetylation and recrystallisation from acetone–hexane afforded the ketone (6) (80 mg) as needles, m.p. 158—160°, $[\alpha]_D$ +32° (*c* 1·0) (lit.,[4] m.p. 154—156°, $[\alpha]_D$ +32°), identical (mixed m.p.) with an authentic sample.

9β-*Methyl*-11-*oxo*-19-*norpregn*-5(10)-*ene*-3β,20β-*diyl Diacetate* (7).[7]—Jones reagent (7·4N; 0·20 ml) was added to a stirred solution of the hydroxy-diacetate (5) (300 mg) in acetone (5 ml) at 0°. After stirring for a further 10 min the solution was poured into dilute potassium hydrogen carbonate solution at 0° and the product isolated with ether. Recrystallisation from acetone–hexane furnished the *ketone* (7) (240 mg) as needles, m.p. 179—180°, $[\alpha]_D$ +105° (*c* 1·0); $\nu_{max.}$ 1730 (OAc) and 1700 cm^{-1} [C(11)=O]; δ 0·57 and 1·18 (each 3H, s, 9- and 13-Me), 1·16 (3H, d, *J* 6·5 Hz, 20-Me), 2·02 (6H, s, 3β- and 20β-OAc), 2·26 and 2·40 (2H, ABq, *J* 12·5 Hz, 12-H$_2$), and 4·40—5·20 (2H, m, 3α-H and 20α-H) (Found: C, 71·85; H, 8·6. $C_{25}H_{36}O_5$ requires C, 72·1; H, 8·7%).

5β,10β-*Epoxy*-11α-*hydroxy*-9β-*methyl*-19-*norpregnane*-3β,20β-*diyl Diacetate* (11).—*m*-Chloroperbenzoic acid (0·6 g) was added to a solution of the alcohol (5) (1·0 g) in dry

benzene (110 ml) and the mixture was kept at room temperature for 16 h. Ether (100 ml) was then added and the solution washed consecutively with sodium hydrogen sulphite, potassium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated. The residue furnished the 5β,10β-*epoxide* (11) (890 mg) as stout needles, m.p. 171—172° (from ether–hexane), $[\alpha]_D$ −25° (*c* 1·0); $\nu_{max.}$ 3620 (OH) and 1725 cm^{-1} (OAc); δ 0·74 and 1·20 (each 3H, s, 9- and 13-Me), 1·16 (3H, d, *J* 6 Hz, 20-Me), 2·01 and 2·03 (each 3H, s, 3β- and 20β-OAc), 3·78 (1H, dd, $J_{ax,ax}$ 11, $J_{ax.eq}$ 4·5 Hz, 11β-H), and 4·32—5·24 (2H, m, 3α-H and 20α-H) (Found: C, 69·05; H, 9·15. $C_{25}H_{38}O_6$ requires C, 69·1; H, 8·8%).

5α,11α-*Epoxy*-10β-*hydroxy*-9β-*methyl*-19-*norpregnane*-3β,20β-*diyl Diacetate* (12).—*Method A*. A solution (8 ml) of peracetic acid (30%) and sulphuric acid (1%) in acetic acid was added to a solution of the olefin (5) (10 g) in glacial acetic acid (40 ml) and the mixture was set aside at room temperature. G.l.c. over a period of 7 days showed an initial increase in the intensity of a peak which was coincident with that of the 5β,10β-epoxide (11), followed by a complete transformation to a compound with a greater retention time. The reaction mixture was poured into aqueous sodium hydrogen sulphite and extracted with ether; the extract was washed with water, dried (Na_2SO_4), and evaporated. The residue gave the 5α,11α-*epoxide* (12) (6·25 g) as needles, m.p. 226—231° (from aqueous methanol), $[\alpha]_D$ +42° (*c* 1·0); $\nu_{max.}$ 3610 (OH) and 1730 cm^{-1} (OAc); δ 0·82 and 1·12 (each 3H, s, 9- and 13-Me), 1·12 (3H, d, *J* 6·5 Hz, 20-Me), 1·98 (6H, s, 3β- and 20β-OAc), 3·85 (1H, d, *J* 6 Hz, 11β-H), and 4·40—5·15 (2H, m, 3α-H and 20α-H) (Found: C, 68·95; H, 8·95. $C_{25}H_{38}O_6$ requires C, 69·1; H, 8·8%).

Method B. When the concentration of the sulphuric acid in method A was 0·30 rather than 0·15%, the reaction was complete in 18 h, affording the same product (g.l.c.).

Method C. A solution (0·008 ml) of peracetic acid (30%) and sulphuric acid (1%) in acetic acid was added to a solution of the 5β,10β-epoxide (11) (10 mg) in glacial acetic acid (0·2 ml). G.l.c. and t.l.c. after 18 h showed complete conversion into the 5α,11α-epoxide (12).

Method D. Complete conversion of (11) into the 5α,11α-epoxide (12) had occurred after 18 h when the procedure of method B was carried out without the peracetic acid.

5α,11α-*Epoxy*-9β-*methyl*-19-*norpregn*-1(10)-*ene*-3β,20β-*diyl Diacetate* (13).—Thionyl chloride (2·6 ml) was added to a solution of the 5α,11α-epoxide (12) (5·15 g) in pyridine (50 ml). The flask was fitted with a drying tube ($CaCl_2$) and kept at room temperature until the dehydration was adjudged (t.l.c.) to be complete (*ca.* 3 h). The mixture was poured into water and the product isolated with ether to give the *olefin diacetate* (13) (3·5 g) as needles, m.p. 155—156° (from acetone–hexane), $[\alpha]_D$ +53° (*c* 0·8); $\nu_{max.}$ 1725 cm^{-1} (OAc); δ 0·88 and 1·29 (each 3H, s, 9- and 13-Me), 1·15 (3H, d, *J* 6 Hz, 20-Me), 2·00 (6H, s, 3β- and 20β-OAc), 3·30 (1H, d, *J* 5·5 Hz, 11β-H), 4·85 (1H, m, $W_{\frac{1}{2}}$ 20 Hz, 3α-H), 5·20 (1H, m, 20α-H), and 5·32 (1H, pseudo-t, *J* 4 Hz, 1-H) (Found: C, 71·75; H, 8·9. $C_{25}H_{36}O_5$ requires C, 72·1; H, 8·7%).

5α,11α-*Epoxy*-9β-*methyl*-19-*norpregn*-1(10)-*ene*-3β,20β-*diol* (14).—Potassium hydroxide (3·7 g) was added to a solution of the olefin (13) (2·4 g) in methanol (120 ml) and the mixture was refluxed for 3 h. The solution was concentrated under reduced pressure and poured into water. The precipitate was filtered off, washed with water at 0° until alkali-free, and recrystallised from aqueous methanol to give the *diol* (14) (1·4 g) as stout needles, m.p. 197—218° (decomp.), $[\alpha]_D$ (EtOH) +7° (*c* 0·8); $\nu_{max.}$ (KCl) 3260 cm^{-1} (OH) (Found: C, 75·65; H, 9·55. $C_{21}H_{32}O_3$ requires C, 75·85; H, 9·7%).

5α,11α-*Epoxy*-10β-*hydroxy*-9β-*methyl*-3-*oxopregnan*-20β-*yl Acetate* (18).—Potassium carbonate (200 mg) was added to a solution of the diacetate (12) (180 mg) in ethanol (25 ml) and the solution was boiled for 0·5 h. Isolation with ether afforded the crude 20-monoacetate (17) (142 mg); $\nu_{max.}$ (KCl) 3396 (OH) and 1732 cm^{-1} (OAc). Jones reagent (8N; 0·04 ml) was added to a solution of the crude monoacetate (17) (100 mg) in acetone (10 ml) at 0°. Isolation with ether yielded the 3-*ketone* (18) (75 mg) as fine needles, m.p. 237—238° (from acetone–hexane), $[\alpha]_D$ +60° (*c* 1·0); $\nu_{max.}$ 3600 (OH) and 1720 cm^{-1} (C=O and OAc); c.d. (dioxan) [θ] +1250; $\lambda_{max.}$ 294 nm; δ 0·83 and 1·23 (each 3H, s, 9- and 13-Me), 1·16 (3H, d, *J* 6·5 Hz, 20-Me), 2·01 (3H, s, 20β-OAc), 3·81 (1H, d, *J* 5·5 Hz, 11β-H), and 4·84 (1H, m, $W_{\frac{1}{2}}$ 20 Hz, 20α-H) (Found: C, 70·75; H, 8·9. $C_{23}H_{34}O_5$ requires C, 70·75; H, 8·8%).

5α,11α-*Epoxy*-9β-*methyl*-19-*norpregn*-1(10)-*ene*-3,20-*dione* (15).—Jones reagent (8N; 1·18 ml) was added dropwise over 10 min with stirring to a suspension of the diol (14) (730 mg) in acetone (200 ml) at 0°. The solution was concentrated under reduced pressure and poured into water. After filtration, the insoluble unchanged crystalline material (200 mg) together with the gum obtained from the filtrate by work-up with ether was re-treated in acetone (200 ml) with Jones reagent (8N; 0·80 ml) with stirring at 0°. The mixture was concentrated under reduced pressure and the product isolated with ether to yield the *dione* (15) (710 mg) (single spot on t.l.c.), as stout needles, m.p. 97—101°; $\nu_{max.}$ 1718 and 1700 cm^{-1} (C=O); δ 0·85, 1·36, and 2·11 (each 3H, s, 9-, 13-, and 20-Me), 2·63 (2H, s, 4-H_2), 2·70 and 3·00 (2H, AB part of ABX system, J_{AB} 22, $J_{AX} = J_{BX}$ = 3·5 Hz, 2-H_2), 3·64 (1H, dd, J_1 6, J_2 1·5 Hz, 11β-H), and 5·5 (1H, pseudo-t *J* 3·5 Hz, 1-H) (Found: M^+, 328·2028. $C_{21}H_{28}O_3$ requires *M*, 328·2038).

3,11α-*Dihydroxy*-9β-*methylpregna*-1,3,5(10)-*trien*-20-*one* (19).—Potassium hydroxide (5N; 0·30 ml) was added to a solution of the foregoing crude dione (15) (650 mg) in ethanol (12 ml). The mixture was set aside for 30 s, neutralised with dilute hydrochloric acid, and concentrated under reduced pressure. The product was isolated with ether to yield a crude solid (640 mg). Recrystallisation from acetone–hexane furnished the *triene* (19) (490 mg) as needles, m.p. 216—217°, $[\alpha]_D$ (EtOH) +55° (*c* 1·0); $\lambda_{max.}$ (EtOH) 218 and 280 nm (ε 15,000 and 3700); $\nu_{max.}$ (Nujol) 3578, 3480, and 3280 (OH), 1685 (C=O), and 1610 and 1500 cm^{-1} (aromatic); δ ($CDCl_3$–CD_3OD) 0·77, 1·38, and 2·10 (each 3H, s, 9-, 13-, and 20-Me), 3·98 (1H, dd, $J_{ax,ax}$ 11, $J_{ax.eq}$ 4 Hz, 11β-H), 6·57 (1H, s, 4-H), 6·65 (1H, dd, $J_{2,1}$ 9, $J_{2,4}$ 2·5 Hz, 2-H), and 8·16 (1H, d, $J_{1,2}$ 9 Hz, 1-H) (Found: C, 76·9; H, 8·85. $C_{21}H_{28}O_3$ requires C, 76·8; H, 8·6%).

We thank Dr. A. J. M. Weber for n.m.r. measurements, Dr. W. McMeekin for t.l.c., g.l.c., and elemental analyses and for i.r. and u.v. spectra, Dr. P. Bladon (Strathclyde University) for mass spectra, and Dr. J. F. Biellmann (Strasbourg University) for the c.d. measurement.

[4/634 *Received*, 27*th March*, 1974]