18-Norpregna-8,11,13-trienes. Part 2.[1] Preparation from 17β-Methyl-17α-pregn-13-enes

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17,17-Dimethyl-18-nor-5β-androsta-8,11,13-trien-3α-yl acetate (6) has been prepared from 9α,11α-epoxy-17α-methyl-5β-androstane-3α,17β-diol 3-acetate (5) in good yield. An attempt to repeat the aromatisation with the analogous 9α,11α-epoxy-5β-pregnane-3α,17α,20β-triol 3,20-diacetate (10) did not give the expected product. However, a number of ring-C-aromatic pregnanes have been successfully prepared from derivatives of 5β-pregnane-3α,11β,17α,20β-tetraol (21). Attempts to aminate some of these aromatic pregnanes at the 3- and 20-positions are described.

PREVIOUS papers from our laboratories have described the preparation of an 18-norpregna-8,11,13-triene [1] and 18-norandrosta-8,11,13-trienes.[2-5] In continuation of the study to evaluate the biological activities of ring-C-aromatic steroids, some other novel syntheses of ring-C-aromatic pregnanes have been developed and are described herein.

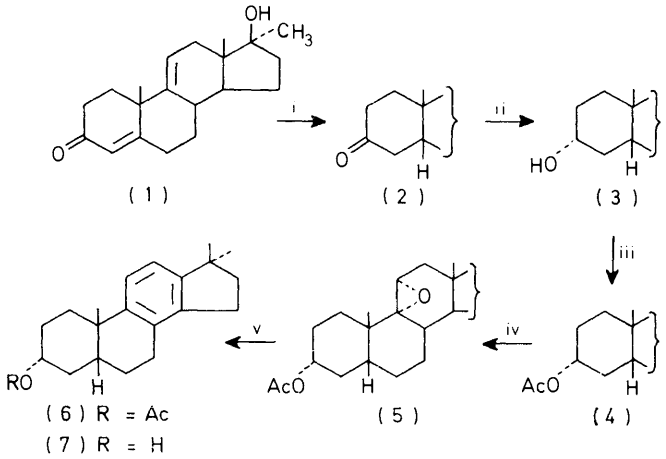
Aromatisation of ring C of a steroid necessitates the removal or migration of the 13β-methyl group. There are a number of examples [2-6] of the concomitant shift of the 13-methyl group of a 17-hydroxy-steroid by way of a Wagner–Meerwein rearrangement to give the 17β-methyl-13-ene. It seemed that application of this rearrangement to 17α-hydroxypregnanes containing one or two potential double bonds in ring C might lead to an efficient route to ring-C-aromatic pregnanes.

We have found that treatment of 9α,11α-epoxy-17α-methyl-5β-androstane-3α,17β-diol 3-acetate (5) with boron trifluoride–ether complex in benzene affords, in high yield, a ring-C-aromatic derivative (6) identical with the acetate prepared from the known [3] 17,17-dimethyl-18-nor-5β-androsta-8,11,13-trien-3α-ol (7).

The hitherto unknown epoxy-acetate (5) was prepared from 17β-hydroxy-17α-methylandrosta-4,9(11)-dien-3-one (1) [7] by the reaction sequence (1) ⟶ (5). The 5β-configuration is assigned to the reduction product (2) because it is known [8] that catalytic hydrogenation of the double bond of steroidal Δ^4-3-ketones under alkaline conditions favours attack from the β-face. Moreover, the observed chemical shift value (δ 1.09) for the C-19 protons of the acetate (4) is in agreement with the

[1] Part 1, C. L. Hewett, J. Redpath, and D. S. Savage, *J.C.S. Perkin I*, 1975, 1288.
[2] C. L. Hewett, S. G. Gibson, I. M. Gilbert, J. Redpath, and D. S. Savage, *J.C.S. Perkin I*, 1973, 1967.
[3] C. L. Hewett, I. M. Gilbert, J. Redpath, D. S. Savage, J. Strachan, T. Sleigh, and R. Taylor, *J.C.S. Perkin I*, 1974, 897.
[4] C. L. Hewett, S. G. Gibson, J. Redpath, and D. S. Savage, *J.C.S. Perkin 1*, 1974, 1432.
[5] C. L. Hewett, S. G. Gibson, I. M. Gilbert, J. Redpath, D. S. Savage, T. Sleigh, and R. Taylor, *J.C.S. Perkin I*, 1975, 336.
[6] N. L. Wendler in ' Molecular Rearrangements Part 2,' ed. P. de Mayo, Interscience, 1964, p. 1020.
[7] M. E. Herr, J. A. Hogg, and R. H. Levin, *J. Amer. Chem. Soc.*, 1956, **78**, 500.
[8] D. M. Kirk and M. P. Hartshorn, ' Steroid Reaction Mechanisms,' Elsevier, Amsterdam, 1968, 81.

Zurcher [9] value of δ 1.10 and is significantly different from the calculated value of δ 0.967 for the 5α-epimer. Confirmation that the 3-hydroxy-group in the diol (3) has the α-configuration was obtained from the ^{1}H n.m.r. spectrum of the acetyl derivative (4), in which the broad

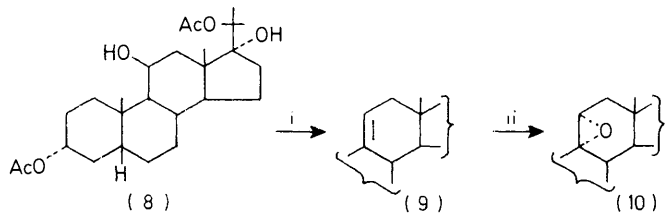


Reagents: i, KOH, MeOH, Pd–$CaCO_3$,H_2; ii, $NaBH_4$,MeOH; iii, Ac_2O,C_5H_5N; iv, AcOH,AcOOH; v, BF_3,Et_2O,C_6H_6

signal ($W_{\frac{1}{2}}$ 17 Hz) at δ 4.70 establishes the 3-proton as axial.[10]

Epoxidation of the acetate (4) with peracetic acid gave the expected [11,12] epoxy-acetate (5). The 9α,11α-configuration for the epoxy-function was confirmed by the downfield shifts in the resonances of the C-18 and C-19 protons (0.07 and 0.06 p.p.m., respectively) which attends the conversion of the 9(11)-ene (4) into the epoxide (5). The shifts are in accord with the Zurcher values.[9]

Having established that the foregoing aromatisation of the 17β-hydroxy-9α,11α-epoxide (5) proceeds in good yield, we decided to investigate the reaction of 9α,11α-epoxy-5β-pregnane-3α,17α,20β-triol 3,20-diacetate (10) with boron trifluoride–ether in benzene. Because the 17-hydroxy and 13-methyl groups in (10) are in the



Reagents: i, $MeSO_2Cl$, SO_2, collidine,DMF; ii, AcOH, AcOOH

trans-quasidiaxial arrangement, it was expected that the aromatisation of ring C would occur with even greater ease than it did with (5). The required epoxy-pregnane (10) was prepared from 5β-pregnane-3α,11β,17α,20β-tetraol 3,20-diacetate (8) [13] by dehydration with methanesulphonyl chloride and sulphur dioxide in collidine–dimethylformamide [14] to give the 9(11)-ene (9) (71% yield), which was epoxidised with peracetic acid. From the ^{1}H n.m.r. spectrum of the dehydration product, the presence of only one olefinic hydrogen atom and the absence of C*H*OH confirms the location of the double bond at the 9(11)- and not at the 12- or 16-position. The α-configuration for the epoxy-function in (10) was confirmed from the downfield ^{1}H n.m.r. shifts of the C-18 and C-19 protons (0.05 and 0.06 p.p.m., respectively) which accompanied the formation of the epoxide from the 9(11)-ene (9).[9]

Attempts to aromatise ring C in the epoxide (10) by treatment with (*a*) boron trifluoride, (*b*) a mixture of acetic anhydride and acetic acid containing toluene-*p*-sulphonic acid, or (*c*) perchloric acid gave intractable complex mixtures.

In a further attempt to find an effective process for the aromatisation, the Δ^{13}-triacetate (11) was prepared from the diacetate (8) essentially by the method described by Herzog and his co-workers.[13] On the evidence of ^{1}H n.m.r. spectroscopy, then in its infancy, these workers located the double bond at C-12, one of the low field signals being assigned to the C-12 olefinic proton. Further investigation of this compound has established that the double bond is in fact at C-13; characteristic upfield chemical shifts of the low-field signals (3β-, 11α-, and 20α-H) occur on conversion of the triacetate (11) into the triol (17).

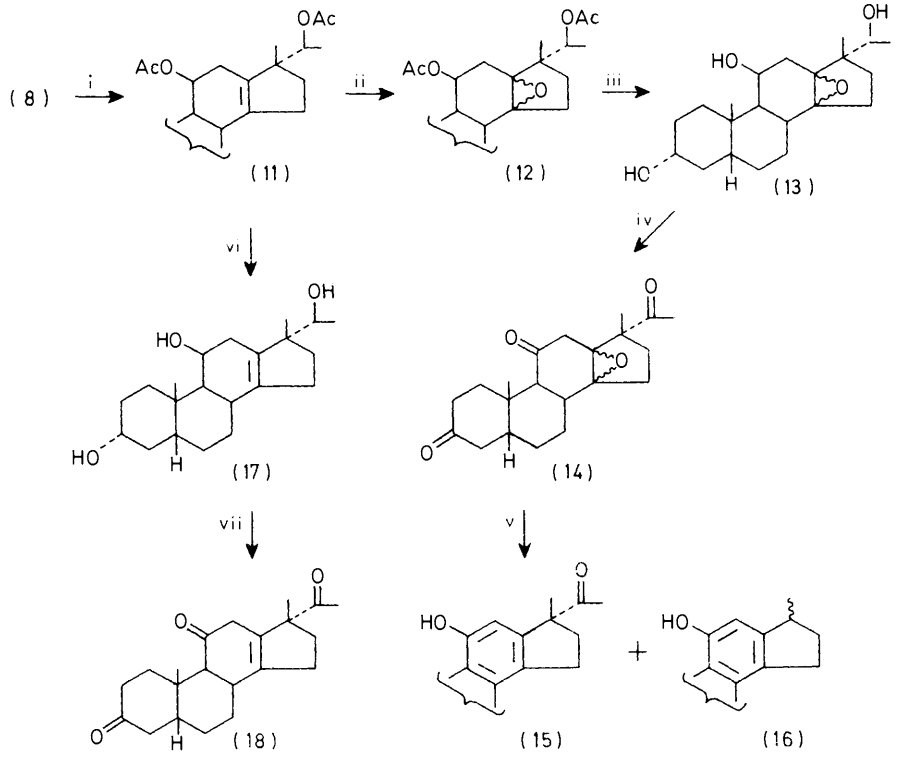
The assignment of the tetrasubstituted double bond to the 13-position in preference to the 8- or 8(14)-positions, either of which could have resulted from further backbone 1,2-hydride shifts following the initial methyl migration, is based on the ^{1}H n.m.r. spectrum of the epoxy-trione (14). The latter was synthesised from the triacetate (11) by the reaction sequence (11) ⟶ (14). The signal for the C-12 methylene group is a well defined AB quartet (δ 2.64 and 2.90; *J* 18 Hz) which establishes the absence of a hydrogen atom at C-13 and hence that the epoxy-group in (14) and the double bond in (11) are at C-13. This AB quartet, which is masked by other signals in the spectrum, is readily discernible by the use of the shift reagent $Eu(fod)_3$. It was also observed that although the signal for the 17β-methyl group underwent a large downfield shift in the presence of $Eu(fod)_3$, no resolution of the signal occurred. From this it is concluded that the epoxide (14) is homogeneous, although the configuration of the epoxy-group is unknown. The sharp singlets for the two angular methyl groups in the ^{1}H n.m.r. spectrum of the intermediate epoxy-triacetate (12) supports this conclusion. Confirmation that the tetrasubstituted double bond in (11) does not reside at C-8 was provided by converting it into the trione (18).

[9] N. S. Bhacca and D. H. Williams, 'Application of NMR Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 13.
[10] Ref. 9, p. 79.
[11] H. Hieymann and L. F Fieser, *J. Amer. Chem. Soc.*, 1951, **73**, 5232.
[12] T. Koga and M. Tomoeda, *Tetrahedron*, 1970, **26**, 1043.
[13] H. L. Herzog, C. C. Joyner, M. J. Gentles, M. T. Hughes, E. P. Oliveto, E. B. Hershberg, and D. H. R. Barton, *J. Org. Chem.*, 1957, **22**, 1413.
[14] G. G. Hazen and D. W. Rosenburg, *J. Org. Chem.*, 1964, **29**, 1930.

This compound does not absorb in the u.v. above 208 nm and hence does not contain an 8-en-11-one grouping. The absence of a singlet for the C-9 hydrogen atom in the ^{1}H n.m.r. spectrum of the epoxy-trione (14) confirms that the double bond is not at the 8(14)-position.

Treatment of the epoxy-trione (14) with formic acid afforded 11-hydroxy-17β-methyl-18-nor-5β,17α-pregna-8,11,13-triene-3,20-dione (15) in 41% yield. U.v. absorption at 293 nm (ε 3 560) indicates a benzenoid ring system, and this is supported by i.r. absorptions at 1 605 and 1 590 cm^{-1}: absorptions at 3 590 and 3 350 cm^{-1} confirm the presence of a hydroxy-group. Confirmatory evidence for structure (15) was obtained from carbonyl groups, and the absorptions at 1 610 and 1 599 cm^{-1} confirm the presence of the aromatic ring.

In view of our interest in the biological activity of aromatic amino-steroids, we wished to prepare amino-derivatives from the dione (15). The 20-derivative was of particular interest because it contains the biologically interesting phenethylamine moeity. An attempt to prepare the 3,20-diamino-derivative of (15) by the Leuckart reaction gave an intractable mixture. Selective reduction of (15) to the ketols, from which monoamines and diamines could have been prepared in a stepwise manner, also failed owing to lack of regio- and stereospecificity. Attempts were then made to prepare the



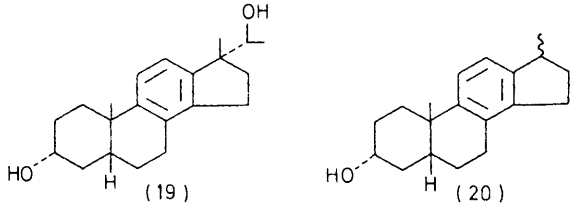
Reagents: i, *p*-MeC$_6$H$_4$·SO$_3$H, AcOH, Ac$_2$O; ii, AcOH, AcOOH; iii, KOH, MeOH; iv, H$_2$CrO$_4$, Me$_2$CO; v, HCO$_2$H; vi, KOH, MeOH; vii, H$_2$CrO$_4$,Me$_2$CO

its ^{1}H n.m.r. spectrum, which displays singlets for the aromatic proton and the 20-, 17β-, and 10β-methyl groups.

In addition to the dione (15), treatment of the epoxy-trione (14) with formic acid gave a monoketone, isolated in 8% yield, which we formulate as 11-hydroxy-17ξ-methyl-18-nor-5β-androsta-8,11,13-trien-3-one (16) on the basis of the following evidence. The monoketone absorbs in the u.v. at 290 nm (ε 3 740) and the mass spectrum displays a molecular ion at *m/e* 284.177 6 ($C_{19}H_{24}O_2$, in agreement with the elemental analysis) which is most readily explained by loss of the 17-acetyl group during aromatisation. This was confirmed by the ^{1}H n.m.r. spectrum, which also shows two methyl signals, one a singlet at δ 1.52 (10β-CH_3) and the other a doublet at δ 1.22 (*J* 6.5 Hz, 17β-CH_3). I.r. bands at 3 595 and 1 715 cm^{-1} are assigned to the hydroxy and

amines by an alternative route *via* the ring-c-aromatic 3,20-diols.

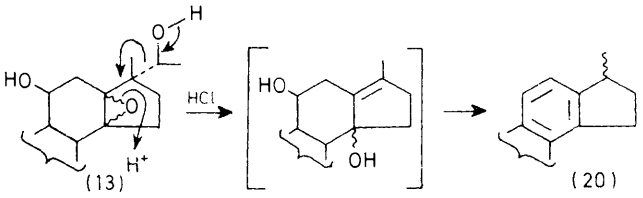
Treatment of an ethanolic solution of the triol epoxide (13) with hydrochloric acid gave a mixture containing two



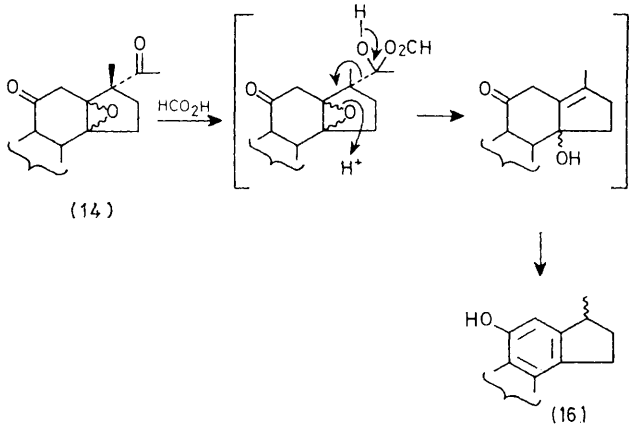
major components. The more polar component, isolated in 57% yield, was a diol, having a molecular ion at *m/e* 314.224 7 ($C_{21}H_{30}O_2$), and formulated as 17β-methyl-5β,17α-pregna-8,11,13-triene-3α,20β-diol (19). This

assignment is based on the ^{1}H n.m.r. spectrum, which displays signals for two carbinol protons at δ 3.67 (m, 3β-H) and 3.93 (q, 20α-H), an AB quartet for the two aromatic protons at δ 6.94 and 7.14 (11- and 12-Hs), a singlet for two methyl groups at δ 1.18 (10β- and 17β-CH_3), and a methyl doublet at δ 1.16 (J 6 Hz, 20-CH_3). By chromatography of the foregoing mixture, another component was isolated (24% yield) which exhibited a molecular ion at m/e 270.198 2 ($C_{19}H_{26}O$) and absorbed in the u.v. at 270 nm (ε 580). This compound is formulated as 17ξ-methyl-5β-androsta-8,11,13-trien-3α-ol (20). The ^{1}H n.m.r. spectrum displays signals for one carbinol proton at δ 3.70 (m, 3β-H) and two methyl groups at δ 1.17 (s, 10β-CH_3) and 1.26 (d, J 6 Hz, 17ξ-H), and an AB quartet for two aromatic protons at δ 6.96 and 7.11 (11- and 12-H).

Whereas the mechanisms by which the triol (13) and the trione (14) are converted by acid into the ring-C-aromatic steroids (19) and (15), respectively, can be



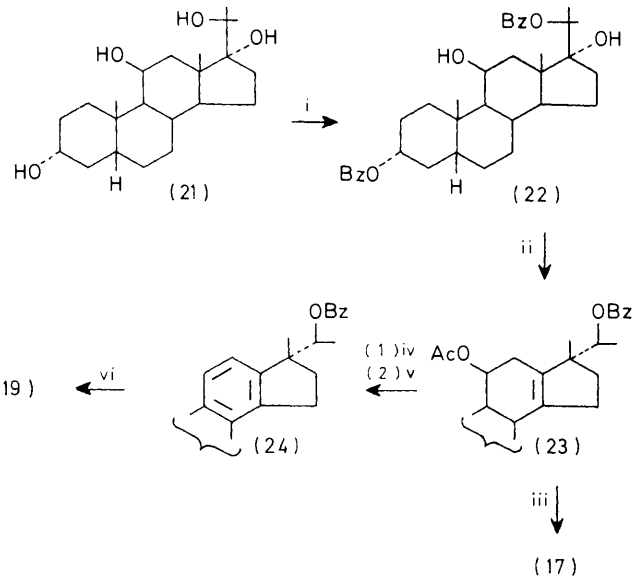
SCHEME 1



SCHEME 2

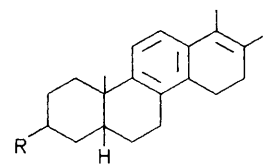
explained readily, the modes of formation of the by-products (20) and (16) produced in the respective reactions are not so obvious. Possible mechanisms by which the side chain is lost from the triol (13) and the trione (14) are suggested in Schemes 1 and 2. Since aromatisation of ring C would be expected to proceed immediately the epoxy-groups in triol (13) and trione (14) are opened in the presence of acid, we suggest that the by-products (20) and (16) result from a concerted reaction involving loss of the side chain concomitant with the opening of the epoxy-groups. If this is true, then the required stereochemistry of the side chain and the epoxy-group is *trans*, *i.e.* the epoxy group has the β-configuration.

Another route to the ring-C-aromatic diol (19) which we explored involved bromination–dehydrobromination



Reagents: i, $PhCOCl,C_5H_5N$; ii, p-$MeC_6H_4{\cdot}SO_3H$, AcOH, Ac_2O; iii, KOH, MeOH; iv, Br_2,CH_2Cl_2; v, NaI, Me_2CO; vi, KOH, MeOH

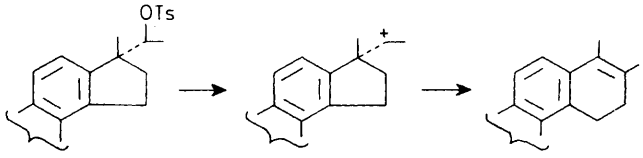
of the 13-olefin (23) by the method developed by Hewett and his co-workers.[3] The dibenzoate (22), obtained from the known tetraol (21) [13] by selective benzoylation, was treated with acetic anhydride in acetic acid containing toluene-p-sulphonic acid according to the method described by Herzog [13] for the diacetate (8) to give 17β-methyl-18-nor-5β,17α-pregn-13-ene-3α,11β,20β-triol 11-acetate 3,20-dibenzoate (23). The structure (23) was confirmed by hydrolysis to the unsaturated triol (17), identical with the triol obtained by hydrolysis of triacetate (11). Treatment of the 13-ene (23) with bromine and then sodium iodide gave, in 48% yield, the ring-C-aromatic dibenzoate (24), which on hydrolysis gave a diol identical with 17β-methyl-5β,17α-pregna-8,11,13-triene-3α,20β-diol (19). The triacetate (11) was also aromatised in good yield (g.l.c.) by the bromination–dehydrobromination procedure, but whereas the dibenzoate (24) crystallised from the crude product, isolation of the corresponding diacetate required chromatography.



(25) R = α—OTs
(26) R = β—N_3
(27) R = β—NH_2
(28) R = β—NHAc

Treatment of the diol (19) with toluene-p-sulphonyl chloride in pyridine gave an intractable gum, which was treated with sodium azide in N-methylpyrrolidone, and the product was then reduced with lithium aluminium hydride. Acetylation of the basic fraction gave a monoacetamide formulated as 3β-acetamido-17,17α-dimethyl-18-nor-D-homo-5β-androsta-8,11,13,17-tetraene

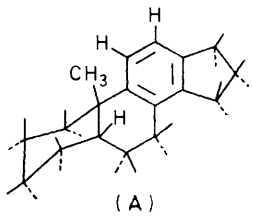
(28) on the following evidence. The mass spectrum displays a molecular ion at *m/e* 337.239 9 ($C_{23}H_{31}NO$): a signal at $M - H_2$ is indicative of the dihydronaphthalene system in the formulated structure.



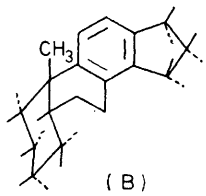
SCHEME 3

The ^1H n.m.r. spectrum shows signals for two vinylic methyl groups at δ 1.90 and 1.98 which suggests that ring-D homoannulation has occurred. This view was confirmed by the u.v. spectrum ($\lambda_{max.}$ 275 nm; ε 12 500) which indicates the presence of a double bond conjugated with the aromatic ring. The mechanism of the D-homoannulation can be rationalised as in Scheme 3.

The half-band width (19 Hz) of the signal for the 3α-H in the acetamide (28) at δ 3.95 was perplexing since conversion of the 3α-tosyloxy-group in the intermediate (25) into the 3-azido group was expected to include inversion, leading to an amido-function [in (28)] with an axial configuration. Even if we accept the possibility that the 3-proton is coupled with the adjacent NH group, the width of the band is too large for a 3-proton with an equatorial configuration and it seemed therefore that the formation of the azide (26) had occurred with retention of configuration. Dreiding models, however, revealed that in 5β-ring-C-aromatic steroids, ring A can readily adopt two different chair conformations (A) and (B). In the former, the 3β-position has the equatorial configuration, while in the latter the 3α-position is equatorial. These models also indicate that there is little difference in energy between the two conformations and it is suggested that in 5β-ring-C-aromatic steroids (and *a priori* steroidal 5β-8-enes) with a bulky group at position 3, ring A may adopt the conformation in which the 3-substituent assumes the equatorial or quasiequatorial configuration.

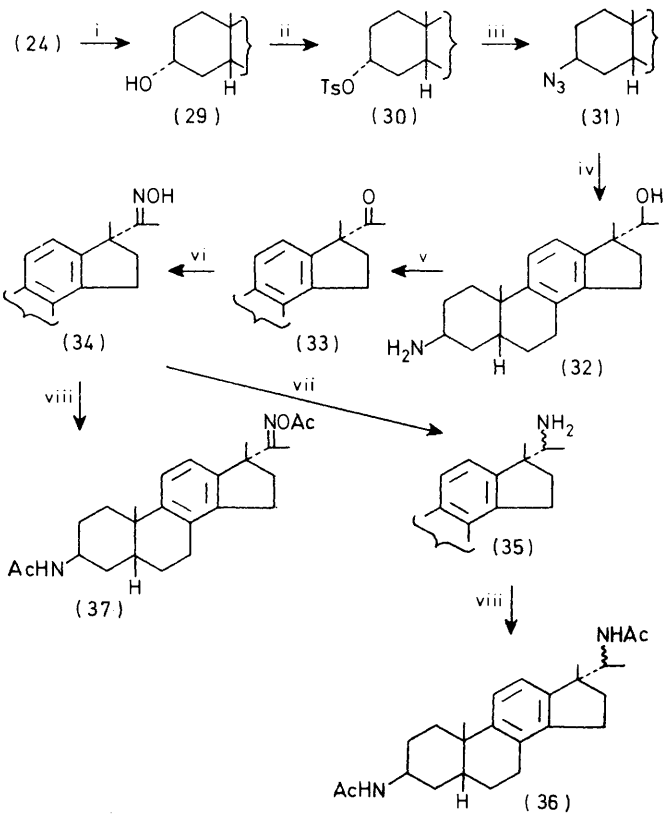


(A)



(B)

Since attempts at the direct 3,20-diamination of both the dione (15) and the diol (19) were unsuccessful, a stepwise diamination process was investigated. Selective hydrolysis of the dibenzoate (24) gave a monohydroxy-derivative, confirmed as the expected 3α-hydroxy-derivative (29) by retention of the quartet at δ 5.23 (*J* 6 Hz) for the C-20 hydrogen atom. This alcohol (29) was converted by the unexceptional sequence of reactions (29) → (34) into 3β-amino-17β-methyl-5β,17α-pregna-8,11,13-trien-20-one oxime (34), which was characterised as the diacetyl derivative (37). The oxime (34) could not be reduced with lithium aluminium hydride but reduction was successfully accomplished with sodium and propan-2-ol to give a non-crystallisable mixture of the 20α- and 20β-amino-derivatives (35) (1 : 1). This mixture could not be resolved even after



Reagents: i, KOH, EtOH; ii, *p*-$MeC_6H_4{\cdot}SO_2Cl$, C_5H_5N; iii, NaN_3, *N*-methylpyrrolidone; iv, $LiAlH_4$,THF; v, H_2CrO_4, AcOH; vi, NH_2OH,HCl, $NaHCO_3$, H_2O, MeOH; vii, Na, Pr^nOH; viii, C_5H_5N, Ac_2O

conversion into the diacetates (36) and exhaustive crystallisation.

EXPERIMENTAL

M.p.s were determined with 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 [^2H]chloroform with a Varian A60 instrument. 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 with a Pye Unicam 105 gas chromatograph (3% SE 30 column at 227 °C; gas flow rate 35 ml $min.^{-1}$)

Concentrations (*c*) are quoted in g per 100 ml. Ether refers to diethyl ether.

17β-*Hydroxy*-17α-*methyl*-5β-*androst*-9(11)-*en*-3-*one* (2).—17β-Hydroxy-17α-methylandrosta-4,9(11)-dien-3-one (1) [7] (34 g) was added to a solution of potassium hydroxide (3.4 g) in methanol (1 200 ml) containing palladium on calcium carbonate (5%) (5 g) and the mixture was shaken under hydrogen until 1.02 mol. equiv. of hydrogen had been absorbed. The catalyst was removed and the mixture was evaporated to dryness. The residual gum (33.8 g) was chromatographed on a column of silica and the fraction eluted with benzene (32 g) recrystallised from ether to give the *ketone* (2) (15.6 g) as plates, m.p. 136—137°, $[\alpha]_D$ −12° (*c* 1.2); $\nu_{max.}$ 3 616 (OH) and 1 715 cm^{-1} (C=O); δ 0.84, 1.16, and 1.24 (each 3 H, s, 13-, 10- and 17-Me) and 5.62 (1 H, d, *J* 6.5 Hz, 11-H) (Found: C, 79.5; H, 10.3. $C_{20}H_{30}O_2$ requires C, 79.4; H, 10.0%).

17α-*Methyl*-5β-*androst*-9(11)-*ene*-3α,17β-*diol* (3).—A solution of the ketone (2) (11.3 g) in methanol (160 ml) at 0 °C was reduced with sodium borohydride (2.9 g). The solution was neutralised with acetic acid and the mixture was poured into water (1 200 ml) at 0 °C. The precipitated solid was washed, dried, and recrystallised from acetone–hexane to afford the *diol* (3) (10.6 g) as plates, m.p. 187—188°, $[\alpha]_D$ 0° (*c* 1.0); $\nu_{max.}$ 3 618 cm^{-1} (OH) (Found: C, 78.9; H, 10.75. $C_{20}H_{32}O_2$ requires C, 78.9; H, 10.6%).

17α-*Methyl*-5β-*androst*-9(11)-*ene*-3α,17β-*diol* 3-*Acetate* (4).—Prepared by acetylation of the diol (3) with acetic anhydride–pyridine, this *acetate* gave plates, m.p. 142—143° (from acetone–hexane), $[\alpha]_D$ +23° (*c* 1.2); $\nu_{max.}$ 3 616 (OH) and 1 730 cm^{-1} (OAc); δ 0.78, 1.09, and 1.22 (each 3 H, s, 13, 10-, and 17-Me), 1.98 (3 H, s, 3α-OAc), 4.70 (1 H, m, $W_{\frac{1}{2}}$ 17 Hz, 3β-H), and 5.42 (1 H, d, *J* 6 Hz, 11-H) (Found: C, 76.2; H, 10.0. $C_{22}H_{34}O_3$ requires C, 76.25; H, 9.9%).

9α,11α-*Epoxy*-17α-*methyl*-5β-*androstane*-3α,17β-*diol* 3-*Acetate* (5).—A solution (18 ml) of commercial peracetic acid (30%) in acetic acid was added to a solution of the olefin (4) (4.4 g) in glacial acetic acid (120 ml). The mixture was set aside for 3 days at room temperature, then poured into aqueous sodium hydrogen sulphite, and the resultant precipitate was filtered off, washed with hot water, and recrystallised from ether–petroleum (b.p. 60—80°) to afford the *epoxide* (5) (2.9 g) as needles, m.p. 161—163°, $[\alpha]_D$ +7° (*c* 1.2); $\nu_{max.}$ 3 610 (OH) and 1 725 cm^{-1} (OAc); δ 0.85 (3 H, s, 13-Me), 1.15 (6 H, s, 10- and 17-Me), 1.96 (3 H, s, 3α-OAc), 3.20 (1 H, d, *J* 4.5 Hz, 11-H), and 4.65 (1 H, m, 3β-H) (Found: C, 72.5; H, 9.4. $C_{22}H_{34}O_4$ requires C, 72.9; H, 9.45%).

17,17-*Dimethyl*-18-*nor*-5β-*androsta*-8,11,13-*trien*-3α-*yl Acetate* (6).—To a solution of the epoxide (5) (0.5 g) in dry benzene (15 ml) was added freshly distilled boron trifluoride–diethyl ether (0.5 ml) and the mixture was stirred for 1.5 h at room temperature. The mixture was poured into aqueous potassium hydrogen carbonate at 0 °C and the product was isolated in the usual manner through ether. Recrystallisation from acetone afforded the *triene* (6) (0.28 g), m.p. 152—153°, $[\alpha]_D$ +70° (*c* 0.8); $\nu_{max.}$ 1 728 cm^{-1} (OAc); δ 1.19 (3 H, s, CH_3), 1.23 (6 H, s, 2 × CH_3), 1.94 (3 H, s, 3α-OAc), 4.84 (1 H, m, $W_{\frac{1}{2}}$ 15 Hz, 3β-H), and 7.00 and 7.10 (2 H, ABq, *J* 9 Hz, 11- and 12-H) (Found: C, 80.6; H, 9.3. $C_{22}H_{30}O_2$ requires C, 80.9; H, 9.25%), identical with the triene obtained by acetylation of 17,17-dimethyl-18-nor-5β-androsta-8,11,13-trien-3α-ol (7) [3] with acetic anhydride–pyridine.

5β-*Pregn*-9(11)-*ene*-3α,17α,20β-*triol* 3,20-*Diacetate* (9).—Methane sulphonyl chloride (15 ml) containing sulphur dioxide (6%) was added to a stirred solution at 0 °C of 5β-pregnane-3α,11β,17α,20β-tetraol 3,20-diacetate (8) [13] (15 g) in dimethylformamide (375 ml) and collidine (150 ml). The temperature of the mixture was allowed to rise to 20 °C and stirring was continued for a further 30 min. The mixture was poured into water (3 l) and the precipitated solid was filtered off, washed thoroughly with water and dried. Recrystallisation from acetone–hexane gave the *olefin* (9) (10.2 g) as needles, m.p. 185—186°, $[\alpha]_D$ +54° (*c* 1.0); $\nu_{max.}$ 3 695 (OH), and 1 740 and 1 730 cm^{-1} (OAc); δ 0.63 and 1.07 (3 H each, s, 10- and 13-Me), 1.25 (3 H, d, *J* 7.5 Hz, 20-Me), 2.00 and 2.04 (3 H each, s, 3α-and 20β-OAc), 5.10 (1 H, q, *J* 7.5 Hz, 20α-H), and 5.38 (1 H, d, *J* 7 Hz, 11-H) (Found: C, 71.8; H, 9.2. $C_{25}H_{38}O_5$ requires C, 71.75; H, 9.15%).

9α,11α-*Epoxy*-5β-*pregnane*-3α,17α,20β-*triol* 3,20-*Diacetate* (10).—A solution (5.25 ml) of commercial peracetic acid (30%) in acetic acid was added to a solution of the olefin (9) (0.7 g) in glacial acetic acid (30 ml). The mixture was kept at room temperature for 5 days, then poured into water at 0 °C, and the precipitated solid was filtered off, washed well with water, sodium hydrogen carbonate solution (5%), and then water again, and dried. Recrystallisation from acetone–hexane furnished the *epoxide* (10) (0.5 g) as prisms, m.p. 210—211°, $[\alpha]_D$ +32° (*c* 1.0); $\nu_{max.}$ 3 590 (OH), 1 735 and 1 725 cm^{-1} (OAc); δ 0.69 and 1.12 (3 H each, s, 13- and 10-Me), 1.18 (3 H, d, *J* 6 Hz, 20-Me), 1.96 and 2.02 (3 H each, s, 3α- and 20β-OAc), 3.17 (1 H, d, *J* 6 Hz, 11β-H), 4.65 (1 H, m, $W_{\frac{1}{2}}$ 17 Hz, 3β-H), and 5.00 (1 H, q, *J* 6 Hz, 20α-H) (Found: C, 69.15; H, 8.55. $C_{25}H_{38}O_6$ requires C, 69.1; H, 8.8%).

17β-*Methyl*-18-*nor*-5β,17α-*pregn*-13-*ene*-3α,11β,20β-*triol Triacetate* (11).—The triacetate was prepared from the diacetate (8) (84 g) by the method described by Herzog *et al.*[13] The product was isolated as a solid by pouring the mixture into water at 0 °C containing a little ether. The solid was filtered off and dissolved in methylene chloride. The solution was washed with water, sodium carbonate solution, and then water again. After removal of the solvent under reduced pressure, recrystallisation from aqueous methanol afforded the triacetate (11) (71 g) as needles, m.p. 123—125°, $[\alpha]_D$ +82° (*c* 1.0) (lit.,[13] m.p. 124—125°, $[\alpha]_D$ +83°); δ 0.91 (6 H, s, 10- and 17-Me), 1.13 (3 H, d, *J* 6 Hz, 20-Me), 1.95 and 1.98 (3 H and 6 H, respectively, s, 3α-,11β-, and 20β-OAc), 4.70 (1 H, m, $W_{\frac{1}{2}}$ 16 Hz, 3β-H), 4.83 (1 H, q, *J* 6 Hz, 20α-H), and 5.35br (1 H, s, 11α-H).

13ξ,14ξ-*Epoxy*-17β-*methyl*-5β,17α-*pregnane*-3α,11β,20β-*triol Triacetate* (12).—A solution (108 ml) of commercial peracetic acid (30%) in acetic acid was added to a solution of the triacetate (11) (70.5 g) in glacial acetic acid (890 ml). The mixture was kept at room temperature overnight then poured into water at 0 °C and the precipitated solid was filtered off, washed with water, sodium hydrogen carbonate solution (5%), and water again, dried, and evaporated under reduced pressure. Recrystallisation from methanol gave the *epoxy-triacetate* (12) (56 g), m.p. 169—171°, $[\alpha]_D$ +88°; $\nu_{max.}$ 1 740, 1 730, and 1 725 (OAc); δ 0.83 and 0.86 (3 H each, s, 17- and 10-Me), 1.20 (3 H, d, *J* 7 Hz, 20-Me), 1.96, 1.99, and 2.03 (3 H each, s, 3α-,11β-, and 20β-OAc), 4.96 (1 H, q, *J* 7 Hz, 20α-H), and 4.40—5.20 (2 H, m, 3β- and 11α-H) (Found: C, 68.0; H, 8.3. $C_{27}H_{40}O_7$ requires C, 68.05; H, 8.45%).

13ξ,14ξ-*Epoxy*-17β-*methyl*-18-*nor*-5β,17α-*pregnane*-3α,11β,20β-*triol* (13).—A solution of potassium hydroxide

(150 g) and the triacetate (12) (55 g) in methanol (900 ml) was boiled for 2 h, concentrated under reduced pressure to about one-fifth of its volume, and then poured into brine. The mixture was extracted with methylene chloride and the organic phase was washed with water until neutral and then dried (Na_2SO_4). Removal of the solvent afforded the crude *epoxy-triol* (13) (43.6 g), $\nu_{max.}$ 3 620 and 3 500 cm^{-1} (OH); δ 0.88 and 1.05 (3 H each, s, 17- and 10-Me), 1.07 (3 H, d, *J* 6 Hz, 20-Me), 3.13br (1 H, s, 11α-H), 3.55 (1 H, m, $W_{\frac{1}{2}}$ 17 Hz, 3β-H), and 3.88 (1 H, q, *J* 6 Hz, 20α-H).

13ξ,14ξ-*Epoxy*-17β-*methyl*-18-*nor*-5β,17α-*pregnane*-3α,-11β,20β-*trione* (14).—Jones reagent (8N; 100 ml) was added in portions over 15 min to a stirred solution of the foregoing crude triol (13) (43 g) in acetone (500 ml) at 0 °C. Stirring was continued until conversion into the trione was complete (t.l.c.) and the solution was concentrated under reduced pressure. The mixture was poured into water and then extracted thrice with ether. The extract was washed with sodium hydrogen carbonate solution and then with water until neutral, and dried (Na_2SO_4). Removal of the solvent and recrystallisation from acetone–hexane gave the *trione* (14) (29 g) as needles, m.p. 150—153°, $[\alpha]_D$ +9° (*c* 1.0); $\nu_{max.}$ 1 725, 1 715, and 1 710 cm^{-1} (C=O); δ 1.13 and 1.20 (3 H each, s, 17- and 10-Me), 2.18 (3 H, s, 17α-OAc), and 2.63 and 2.88 (2 H, ABq, *J* 18 Hz, 11α- and 11β-H) (Found: C, 73.25; H, 8.2. $C_{21}H_{28}O_4$ requires C, 73.2; H, 8.2%).

11-*Hydroxy*-17β-*methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*triene*-3,20-*dione* (15) *and* 11-*Hydroxy*-17ξ-*methyl*-18-*nor*-5β-*androsta*-8,11,13-*trien*-3-*one* (16).—A solution of the epoxy-trione (14) (10 g) was heated under reflux in formic acid (98%; 110 ml) for 0.5 h and then concentrated under reduced pressure. The solution was poured into sodium hydrogen carbonate solution to render the mixture alkaline and then extracted thrice with ether. The extract was washed thrice with water until neutral, dried (Na_2SO_4), and evaporated under reduced pressure to give a gum (10 g). Two crystallisations of this material from acetone–hexane gave the *pregnatriene* (15) (1.65 g), m.p. 190—192°, $[\alpha]_D$ +158°; $\lambda_{max.}$ 293 nm (ε 3 560); $\nu_{max.}$ 3 590 (OH), 3 350br (OH), 1 710 and 1 700 (C=O), and 1 605 and 1 590 cm^{-1} (aromatic ring); δ 1.37 and 1.55 (3 H each, s, 17- and 10-Me), 2.00 (3 H, s, 20-Me) and 6.38 (1 H, s, 12-H) (Found: C, 77.55; H, 8.0%; M^+ 326.188 6. $C_{21}H_{26}O_3$ requires C, 77.3; H, 8.0%; *M* 326.188 2). The mother liquors were combined, evaporated to dryness and the residue was chromatographed on silica using mixtures of toluene and ethyl acetate. The material (730 mg) first eluted from the column was recrystallised from acetone–hexane to give the *androstatriene* (16) (650 mg), m.p. 189—191°, $[\alpha]_D$ +54° (*c* 1.0); $\lambda_{max.}$ 290 nm (ε 3 740); $\nu_{max.}$ 3 595 (OH), 1 715 (C=O), and 1 610 and 1 590 cm^{-1} (aromatic ring); δ 1.22 (3 H, d, *J* 6.5 Hz, 17-Me), 1.52 (3 H, s, 10-Me), and 6.41 (1 H, s, 12-H) (Found: C, 80.55; H, 8.8%; M^+, 284.177 6. $C_{19}H_{24}O_2$ requires C, 80.25; H, 8.5%; *M*, 284.177 6). Subsequent elution afforded a fraction which was recrystallised from acetone–hexane to give a further quantity (2.2 g) of pure pregnatriene (15), m.p. 190—192°.

17β-*Methyl*-18-*nor*-5β,17α-*pregn*-13-*ene*-3α,11β,20β-*triol* (17).—Hydrolysis of the triacetate (11) (500 mg) by the method described by Herzog [13] gave the triol (17) (245 mg), m.p. 158—160°, $[\alpha]_D$ (dioxan) +14° [lit.,[13] m.p. 158—160°, $[\alpha]_D$ (dioxan) +14°]; δ 0.94 and 1.10 (3 H each, s, 10- and 17-Me), 1.08 (3 H, d, *J* 6 Hz, 20-Me), 3.61 (1 H, q, *J* 6 Hz, 20α-H), 3.62 (1 H, m, $W_{\frac{1}{2}}$ 20 Hz, 3β-H), and 4.24br (1 H, s, 11α-H).

17β-*Methyl*-18-*nor*-5β,17α-*pregn*-13-*ene*-3,11,20-*trione* (18).—Jones reagent (7N; 0.50 ml) was added dropwise to a stirred solution of the foregoing triol (17) (200 mg) in acetone (10 ml) at 0 °C. Isolation with ether in the usual way gave the unstable trione (18) (184 mg), which showed no strong u.v. absorption above 208 nm; $\nu_{max.}$ 1 720 and 1 710 cm^{-1} (3 × C=O).

17β-*Methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*triene*-3α,20β-*diol* (19) *and* 17ξ-*Methyl*-18-*nor*-5β-*androsta*-8,11,13-*trien*-3α-*ol* (20).—A mixture of the triol epoxide (13) (23.5 g), concentrated hydrochloric acid (14 ml), and ethanol (700 ml) was heated under reflux for 50 min, then concentrated under reduced pressure. Ether was added and the ethereal solution was washed with water, sodium carbonate, and water again. After drying (Na_2SO_4), the solvent was removed under reduced pressure and the residual gum, which contained two main components, was chromatographed on silica [ether–toluene (1 : 9) to ether–toluene (1 : 1)]. The less polar main component (5.6 g) was recrystallised from acetone–hexane to give the *androstatriene* (20) (4.25 g) as needles, m.p. 133—136°, $[\alpha]_D$ +52° (*c* 1.2); $\lambda_{max.}$ 270 nm (ε 580); $\nu_{max.}$ 3 608 cm^{-1} (OH), δ 1.17 (3 H, s, 10-Me), 1.26 (3 H, d, *J* 6 Hz, 17-Me), 3.70 (1 H, m, $W_{\frac{1}{2}}$ 18 Hz, 3β-H), and 6.96 and 7.11 (2 H, ABq, *J* 7.5 Hz, 11- and 12-H) (Found: C, 84.4; H, 9.7%; M^+, 270.198 2. $C_{19}H_{26}O$ requires C, 84.4; H, 9.7%; *M*, 270.198 4). The other main component was recrystallised from ether–hexane to give the *pregnatriene* (19) (11.8 g) as needles, m.p. 156—157°, $[\alpha]_D$ +12.4° (*c* 1.4); $\lambda_{max.}$ 270 nm (ε 455); $\nu_{max.}$ 3 515 and 3 460 cm^{-1} (OH); δ 1.16 (3 H, d, *J* 6 Hz, 20-Me), 1.18 (6 H, s, 10- and 17-Me), 3.67 (1 H, m, $W_{\frac{1}{2}}$ 19 Hz, 3β-H), 3.93 (1 H, q, *J* 6 Hz, 20α-H), and 6.94 and 7.14 (2 H, ABq, *J* 8 Hz, 11- and 12-H) (Found: C, 80.1; H, 9.7%; M^+, 314.224 7. $C_{21}H_{30}O_2$ requires C, 80.2; H, 9.6%; *M*, 314.224 6).

5β-*Pregnane*-3α,11β,17α,20β-*tetraol* 3,20-*Dibenzoate* (22).—To a solution of the tetraol (21) [13] (40 g) in pyridine (1 800 ml) at 0 °C, benzoyl chloride (90 ml) was added in portions. The mixture was kept at room temperature for 5 days then poured into water at 0 °C and the resulting gummy solid was filtered off and dissolved in ether. The ethereal solution was washed with sodium carbonate and water and then dried (Na_2SO_4). Removal of the solvent afforded a gum which was crystallised from ethanol to yield the *dibenzoate* (22) (53 g), m.p. 220—222°. One recrystallisation from ethanol afforded plates, m.p. 221—223°, $[\alpha]_D$ +82° (*c* 1.3); $\lambda_{max.}$ 230 nm (ε 30 000); $\nu_{max.}$ 3 600 (OH), 1 720, 1 715, and 1 705 (benzoates), and 1 600 and 1 580 cm^{-1} (aromatic); δ 0.99 and 1.16 (3 H each, s, 10- and 13-Me), 1.35 (3 H, d, *J* 6 Hz, 21-Me), 4.20 (1 H, m, $W_{\frac{1}{2}}$ 6 Hz, 11α-H), 4.95 (1 H, m, $W_{\frac{1}{2}}$ 20 Hz, 3β-H), 5.40 (1 H, q, *J* 6 Hz, 20α-H), and 7.25—8.20 (10 H, m, aromatic H) (Found: C, 74.8; H, 7.75. $C_{35}H_{44}O_6$ requires C, 75.0; H, 7.9%).

17β-*Methyl*-18-*nor*-5β,17α-*pregn*-13-*ene*-3α,11β,20β-*triol* 11-*Acetate* 3,20-*Dibenzoate* (23).—To a solution of the dibenzoate (22) (49.5 g) in acetic anhydride (1 : 1; 1 100 ml) was added toluene-*p*-sulphonic acid (9 g). The mixture was set aside at room temperature for 18 h, then poured into water at 0 °C, and the precipitated solid was filtered off and dissolved in ether. The ethereal solution was washed with sodium carbonate solution and then water. Removal of the solvent under reduced pressure and crystallisation from acetone afforded the *acetoxy-dibenzoate* (23) (39 g) as plates, m.p. 183—185°, $[\alpha]_D$ +14.5° (*c* 1.2); $\lambda_{max.}$ 230 nm (ε 22 650); $\nu_{max.}$ 1 725, 1 710, and 1 700 (OAc and OBz), and 1 600,

1 585, and 1 490 cm^{-1} (aromatic); δ 0.91 and 1.01 (3 H each, s, 10- and 17-Me), 1.30 (3 H, d, *J* 6 Hz, 20-Me), 1.96 (3 H, s, 11β-OAc), 4.90 (1 H, m, $W_{\frac{1}{2}}$ 20 Hz, 3β-H), 5.15 (1 H, q, *J* 6 Hz, 20α-H), 5.42 (1 H, m, $W_{\frac{1}{2}}$ 6 Hz, 11α-H), and 7.20—8.25 (10 H, m, aromatic H) (Found: C, 76.05; H, 7.8. $C_{37}H_{44}O_6$ requires C, 76.0; H, 7.6%). The acetoxy-benzoate (23) (100 mg) in methanol (5 ml) containing aqueous potassium hydroxide (4M; 0.5 ml) was heated under reflux for 3 h. Isolation in the usual manner afforded the diol (17), identical with the sample prepared previously.

17β-*Methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*triene*-3α,20β-*diol Dibenzoate* (24).—To a stirred solution of the acetoxy-dibenzoate (23) (18.5 g) in methylene chloride (190 ml) and ether (225 ml) at −55 °C was added a solution of bromine (5 ml) in methylene chloride (10 ml) and the mixture was allowed to warm to −15 °C over 1 h, after which time no starting material was observed (t.l.c.). A solution of sodium iodide (40 g) in acetone (500 ml) was added over 15 min and the mixture was heated under reflux for 2 h. After cooling, sodium hydrogen sulphite solution was added and the product was isolated through ether in the usual manner. Recrystallisation from acetone–hexane afforded the *triene* (24) (7.9 g), m.p. 146—149°, $[\alpha]_D$ +59° (*c* 0.65); $\lambda_{max.}$ 225 and 270 nm (ε 32 000; and 3 900); $\nu_{max.}$ 1 710 (OBz), and 1 605, 1 585, and 1 495 cm^{-1} (aromatic); δ 1.21 and 1.38 (3 H each, s, 10- and 17-Me), 1.32 (3 H, d, *J* 7 Hz, 20-Me), 4.95 (1 H, m, $W_{\frac{1}{2}}$ 20 Hz, 3β-H), 5.22 (1 H, q, *J* 6 Hz, 20α-H), 7.10 (2 H, s, 11- and 12-H), and 7.20—8.10 (10 H, m, aromatic H) (Found: C, 80.2; H, 7.4. $C_{35}H_{38}O_4$ requires C, 80.4; H, 7.3%).

A mixture of the dibenzoate (24) (1 g) and potassium hydroxide (2 g) in ethanol (20 ml) was boiled for 4.5 h. Isolation in the usual manner with ether and recrystallisation from ether–hexane afforded the diol (19) (0.4 g), identical with the diol obtained previously.

3β-*Acetamido*-17,17α-*dimethyl*-18-*nor*-D-*homo*-5β-*androsta*-8,11,13,17-*tetraene* (28).—17β-Methyl-18-nor-5β-17α-pregna-8,11,13-triene-3α,20β-diol (19) (6 g) and toluene-*p*-sulphonyl chloride (6 g) in pyridine (20 ml) was set aside for 3 days at room temperature, and the mixture was then poured into water at 0 °C. After drying, the precipitated solid [$\nu_{max.}$ 1 360 and 1 180 cm^{-1} ($-SO_2-O-$); δ 4.54 (*ca.* 1.2 H, flat m, 3β-H, + a little 20α-H)] was dissolved in *N*-methyl-2-pyrrolidone (100 ml) containing sodium azide (9 g) and the mixture was stirred at room temperature for 4 h. It was then poured into water and extracted with cyclohexane. After drying (Na_2SO_4), the cyclohexane solution was passed down a short column of silica to afford a gum (4.2 g), $\nu_{max.}$ 2 100vs cm^{-1} (N_3); g.l.c. rel. t_R 0.23, 0.30, 0.61, and 0.82 (cholestane ≡ 1.0). This gum (4.0 g) in tetrahydrofuran (100 ml) was added slowly to a suspension of lithium aluminium hydride (2.5 g) in tetrahydrofuran (50 ml) and the mixture was heated under reflux for 1.5 h in nitrogen. The cooled mixture was slowly added to water at 0 °C. Isolation through ether afforded a gum (3.1 g), g.l.c. rel. t_R 0.23, 0.30, 0.44, and 0.60 (cholestane ≡ 1.0), which was dissolved in ether, and the neutral and basic fractions were separated using hydrochloric acid (N). The neutral fraction (0.5 g) exhibited t_R 0.23 and 0.30. The basic fraction (2.45 g) (t_R 0.44 and 0.60) was acetylated with pyridine–acetic anhydride and the precipitated solid, obtained by dilution with water, was recrystallised from aqueous acetone to give the *acetamide* (28) (0.98 g), m.p. 185—190°, $[\alpha]_D$ −65° (*c* 1.2); $\lambda_{max.}$ 275 nm (ε 12 500); $\nu_{max.}$ 3 450 (NH) and 1 675 cm^{-1} (Ac); δ 1.33 (3 H, s, 10-Me) 1.90 (3 H, s, vinylic Me), 1.98 (6 H, s, Ac and vinylic Me), 3.95 (1 H, m, $W_{\frac{1}{2}}$ 16 Hz, 3α-H), 5.55 (1 H, m, $W_{\frac{1}{2}}$ 18 Hz, 3β-N*H*Ac), and 7.12 (2 H, s, aromatic H) (Found: C, 81.9; H, 9.1; N, 4.1%; M^+ 337.239 7. $C_{23}H_{31}NO$ requires C, 81.85; H, 9.25; N, 4.15%; *M*, 337.240 6).

17β-*Methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*triene*-3α,20β-*diol* 20-*Benzoate* (29).—A mixture of potassium hydroxide (2.4 g) and the dibenzoate (24) (12 g) in ethanol (500 ml) was set aside for 16 h then concentrated to low volume under reduced pressure and poured into water at 0 °C. Isolation of the product through methylene chloride afforded a gum. Chromatography on silica and elution with benzene–ether (9 : 1) afforded the amorphous monobenzoate (29) (4.6 g), $\nu_{max.}$ 3 608 (OH), 1 710 (AcO), and 1 604, 1 585, and 1 490 cm^{-1} (aromatic); δ 1.05 (1 H, s, 3α-OH), 1.14 (3 H, s, 10-Me), 1.25 (3 H, d, *J* 6 Hz, 20-Me), 1.34 (3 H, s, 17-Me), 3.52 (1 H, m, $W_{\frac{1}{2}}$ 20 Hz, 3β-H), 5.23 (1 H, q, *J* 6 Hz, 20α-H), and 7.04—8.00 (7 H, m, aromatic H).

17β-*Methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*triene*-3α,20β-*diol* 20-*Benzoate* 3-*Tosylate* (30).—Toluene-*p*-sulphonyl chloride (5.2 g) was added to a solution of the mono-ol (29) (5.2 g) in pyridine (20 ml) and the mixture was maintained at 5 °C for 24 h. Dilution with water precipitated a solid which was filtered off and dried under reduced pressure to give the *benzoyloxy-tosylate* (30) (6.9 g), m.p. 163—166°, $[\alpha]_D$ +29° (*c* 1.4); $\nu_{max.}$ (KCl) 1 713 (BzO), 1 360 and 1 185 (TsO), and 1 600, 1 585, and 1 498 cm^{-1} (aromatic); δ 1.12 and 1.35 (3 H each, s, 10- and 17-Me), 1.30 (3 H, d, *J* 6 Hz, 20-Me), 2.41 (3 H, s, ArCH_3), 4.50 (1 H, m, $W_{\frac{1}{2}}$ 17 Hz, 3β-H), 5.28 (1 H, q, *J* 6 Hz, 20α-H), and 7.00—8.00 (11 aromatic H) (Found: C, 73.6; H, 7.25; S, 6.1. $C_{35}H_{40}O_5S$ requires C, 73.4; H, 7.05; S, 5.6%).

3β-*Azido*-17β-*methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*trien*-20β-*yl Benzoate* (31).—Sodium azide (4 g) was added to a stirred solution of the tosylate (30) (6 g) in *N*-methyl-pyrrolidone (80 ml) at 90 °C. The mixture was maintained at that temperature for 3 h, then poured into water at 0 °C. Isolation through ether afforded a gummy solid (two spots on t.l.c.) (4.3 g) which was chromatographed on silica. The fractions containing the more polar component [eluted with toluene–ethyl acetate (9 : 1)] were combined and recrystallised from ether–methanol to give the *azide* (31) (1.9 g). A further crystallisation gave a sample, m.p. 110—111°, $[\alpha]_D$ +14°; $\nu_{max.}$ 2 100 (N_3), 1 710 (BzO), and 1 600 and 1 585 cm^{-1} (aromatic); δ 1.22 and 1.36 (3 H each, s, 10- and 17-Me), 1.27 (3 H, d, *J* 6 Hz, 20-Me), 3.52 (1 H, m, $W_{\frac{1}{2}}$ 12 Hz, 3α-H), 5.25 (1 H, q, *J* 6 Hz, 20α-H), and 7.05—8.00 (7 H, m, aromatic H) (Found: C, 76.1; H, 7.6. $C_{28}H_{33}N_3O_2$ requires C, 75.8; H, 7.5%).

3β-*Amino*-17β-*methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*trien*-20β-*ol* (32).—To a stirred suspension of lithium aluminium hydride (0.4 g) in tetrahydrofuran (8 ml) was added dropwise a solution of the azide (31) (1 g) in tetrahydrofuran (8 ml) and the mixture was boiled for 90 min in nitrogen. Water was added slowly to the cooled solution and the mixture was extracted with ether. The ethereal layer was extracted with hydrochloric acid (N) and the resultant aqueous layer was treated with potassium hydroxide solution (N). Extraction with ether afforded the amine (32) (0.9 g) as a gum, $\nu_{max.}$ 3 600 and 3 570 (NH_2 and OH) and 1 608 and 1 585 cm^{-1} (aromatic); δ 1.15 (3 H, d, *J* 6 Hz, 20-Me), 1.17 and 1.34 (3 H each, s, 10- and 17-Me), 3.90 (1 H, q, *J* 6 Hz, 20α-H), and 6.89 and 7.11 (2 H, ABq, *J* 9 Hz, 11- and 12-H).

3β-*Amino*-17β-*methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*trien*-

20-*one* (33).—To a stirred solution of the amine (32) (0.8 g) in glacial acetic acid (12 ml) was added Kiliani reagent (4N; 3 ml). The mixture was stirred for a further 30 min, then poured into aqueous potassium hydroxide (N) at 0 °C. Isolation of the basic material in the usual way with ether, *via* the hydrochloride salt, afforded the unstable amino-ketone (33) (0.7 g) as a gum, $\nu_{max.}$ 3 690 and 3 400 (NH_2), 1 705 (C=O), and 1 642 and 1 582 cm^{-1} (aromatic); δ 1.34 and 1.41 (3 H each, s, 10- and 17-Me), 1.99 (3 H, s, 20-Me), and 6.88 and 7.10 (2 H, ABq, *J* 9 Hz, 11- and 12-H).

3β-*Amino*-17β-*methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*trien*-20-*one Oxime* (34) *and its Diacetate* (37).—To a solution of the amino-ketone (33) (0.6 g) in methanol (20 ml) were added hydroxylamine hydrochloride (0.45 g), sodium hydrogen carbonate (0.65 g), and water (0.5 ml). The mixture was heated under reflux for 3.5 h then cooled and poured into water at 0 °C, and the precipitated solid was filtered off, washed with water, and dried to give the oxime (34) (0.52 g), m.p. 90—110°, $\nu_{max.}$ 3 580 and 3 250br (NH_2 and =NOH) and 1 585 cm^{-1} (aromatic); δ 1.34, 1.42, and 1.72 (3 H each, s, 10-, 17-, and 20-Me) and 6.87 and 7.09 (2 H, ABq, *J* 9 Hz, 11- and 12-H). Acetylation of the oxime (34) with acetic anhydride–pyridine and crystallisation of the product from acetone–ether gave the *diacetate* (37) as white plates, m.p. 105—107°, $[\alpha]_D$ +43° (*c* 1.0); $\lambda_{max.}$ 208 nm (ε 14 400); $\nu_{max.}$ 3 440 (NH), 1 762 (oxime acetate C=O), and 1 673 cm^{-1} (amide C=O); δ 1.31, 1.47, 1.77, 1.94, and 2.13 (3 H each, s, 10-Me, 17-Me, 20-Me, NHAc, and C=NOAc), 2.30—3.00 (4 H, m, 7-H_2 and 14-H_2), 3.60—4.30 (1 H, m, 3α-H), 5.60 (1 H, d, *J* 8 Hz, NH), and 6.86 and 7.08 (2 H, ABq, *J* 8 Hz, 11- and 12-H) (Found: C, 73.0; H, 8.45; N, 6.5. $C_{25}H_{34}N_2O_3$ requires C, 73.1; H, 8.4; N, 6.8%).

Reduction of the Oxime (34) *with Sodium and Propan*-1-*ol*.—Sodium (1.5 g) was added in portions to a boiling solution of the oxime (34) (0.45 g) in propan-1-ol (15 ml) over 3 h. The cooled mixture was added slowly to water at 0 °C and the product was isolated through ether to give a mixture of 20α- and 20β-amines (35) (*ca.* 1 : 1 by g.l.c.) as a gum (0.39 g).

Acetylation of the Mixture of 3β,20α- *and* 3β,20β-*Diamino*-17β-*methyl*-18-*nor*-5β,17α-*pregna*-8,11,13-*triene* (35).—A solution of the mixture of amines (35) (0.38 g) in pyridine–acetic anhydride (2 : 1; 1 ml) was set aside for 1 h at room temperature and then poured into water at 0 °C. The precipitated solid was filtered off, washed with water, dried under reduced pressure, and chromatographed on alumina. Elution with methylene chloride–methanol (50 : 1) and recrystallisation from methanol–water furnished the *bis-acetamide* (36) (0.19 g) as a mixture (*ca.* 1 : 1) of 20α- and 20β-isomers, $\nu_{max.}$ 3 445 and 3 330 (NH), 1 674 (C=O), and 1 510 cm^{-1} (NH); δ 1.02 (1 H, d, *J* 6 Hz, 20-Me), 1.27 and 1.32 (3 H each, s, 10- and 17-Me), 1.87 and 1.91 (3 H, s, 20α- and 20β-NHAc), 1.96 (3 H, s, 3β-NHAc), 3.60—4.45 (2 H, m, 3α-, 20α-, and 20β-H), and 6.89 and 7.11 (2 H, ABq, *J* 9 Hz, 11- and 12-H) (Found: C, 74.05; H, 9.15; N, 6.7%; M^+, 396.276 7. $C_{25}H_{36}N_2O_2$,0.5H_2O requires C, 74.0; H, 9.2; N, 6.9%; *M*, 396.277 7).

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