Steroidal *N*-Nitro-amines. Part 2.[1] Denitroamination of Steroidal 12β-, 17β-, 20β-, and 23*R*-Nitro-amines

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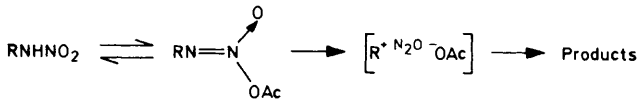
20β-Nitroaminopregn-5-en-3β-yl acetate (13a), 17β-nitroamino-5α-androstan-3β-yl acetate (14), and 12β-nitroamino-(25*R*)-5α-spirostan-3β-yl acetate (15a) have been prepared by nitrosation of the corresponding oximes, followed by reduction with sodium borohydride. The 23-nitro-imine (12), obtained by reaction of sarsasapogenin acetate (10) with nitrous acid and boron trifluoride–diethyl ether complex, was similarly reduced to give 23*R*-nitroamino-(20*S*,22*S*,25*S*)-5β-spirostan-3β-yl acetate (16). Denitroamination of (13a) was achieved by treatment with acetic anhydride and pyridine to give the acetates of pregna-5,20-dien-3β-ol (17), pregn-5-ene-3β,20β-diol (18), 17α-methyl-D-homo-androst-5-ene-3,17aβ-diol (19), and 17α-methyl-12a-methylene-c(12a)-homo-18-norandrost-5-en-3β-ol (20). Under the same conditions the nitro-amine (14) afforded the acetates of 5α-androst-16-en-3β-ol (27a), 17β-methyl-18-nor-5α-androst-12-en-3β-ol (28a), 17-methyl-18-nor-5α-androst-13(17)-en-3β-ol (29a), and 17β-methyl-18-nor-5α-androst-13-en-3β-ol (30a). Denitroamination of (15a) took place through the expected c-nor-D-homo rearrangement producing 14(13 → 12αH)*abeo*-(25*R*)-5α-spirost-13(18)-en-3β-yl acetate (31) in high yield and a minor amount of 14(13 → 12)*abeo*-(25*R*)-5α-spirost-12-en-3β-yl acetate (32). The *trans*-stereochemistry of the β-hydrogen-elimination produced in the denitroamination of (16) was established by using labelled sarsasapogenin (10) biosynthesized by *Agave attenuata* from [2-^{14}C,(4R)-4-^{3}H]mevalonic acid.

In a preceding paper [1] we reported the denitroamination of 4β-, 6β-, 7α-, and 7β-steroidal nitro-amines by treatment with acetic anhydride and pyridine. An ion pair mechanism, similar to that currently accepted for the deamination of alkyl primary amines with nitrous acid,[2] was proposed as shown in Scheme 1.

The observed denitroamination products were olefins produced by a β-elimination process, acetates by substitution for the counter ion, and, in the case of α-hydroxy-nitro-amines, oxirans by intramolecular nucleophilic substitution.

The purpose of the study reported herein was to examine the denitroamination reactions of steroidal nitro-amines in positions 12β-, 20β-, and 17β- of the steroid skeleton in order to compare them with the behaviour of other functional groups in the same positions that are able to generate carbocations, *e.g.* nitrous acid deamination of amines,[3] solvolysis and pyrolysis of tosylates,[3a,4] mesylates,[3a] and sulphates,[5] and dehydration of alcohols.[3a,6] The major products of these reactions are, in general, Wagner-Meerwein type rearranged compounds. We also report the stereochemistry of the β-hydrogen elimination reaction during the denitroamination of the axial 23-nitro-amine (16).



Scheme 1

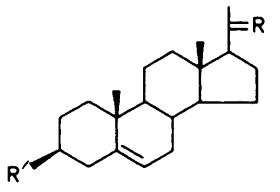
Results and Discussion

Preparation of the Substrates.—20-Nitroiminopregn-5-en-3β-yl acetate (3) was conveniently prepared (78%) by nitrosation [7] of the corresponding oxime (2) with sodium nitrite in methylene chloride–acetic acid. Its i.r. spectrum shows bands characteristic of the nitro-imine group [8] at 1 620 (C=N) and 1 580 and 1 315 cm^{-1} (NO_2). In a similar way 17-nitroimino-5α-androstan-3β-yl acetate (6) and 12-nitroimino-(25*R*)-5α-spirostan-3β-yl acetate (9) were synthesized in 26 and 98% yield, respectively, the analytical and spectroscopic data being in accord with the proposed structures; the low yield observed for the nitro-imine (6) was due to hydrolysis to the ketone (4) (65%) during the reaction. Treatment of (25*S*)-5β-spirostan-3β-yl acetate (sarsasapogenin acetate) (10) with sodium nitrite in acetic acid and boron trifluoride–diethyl ether complex led [9a,b] to a mixture of 23-oxosarsasapogenin acetate (11) (15%) and 23-nitroiminosarsasapogenin acetate (12) (51%). The mass spectrum of (12), which shows the expected fragment corresponding to $M^+ - NO_2$ (*m/z* 470, 33%), has a typical fragmentation pattern of spirostan sapogenin with an electronegative substituent at C-23 [9b,c] (see Experimental section); its i.r. spectrum exhibits absorptions at 1 644 (C=N) and 1 575 and 1 318 cm^{-1} (NO_2). Chemical evidence for this structure was obtained by hydrolysis of (12) with neutral aluminium oxide (activity III) to give quantitatively the ketone (11).

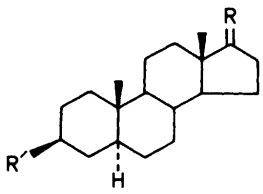
The reduction [8] of the nitro-imines (3), (6), (9), and (12) with sodium borohydride in ethanol at room temperature led to 20β-nitroaminopregn-5-en-3β-yl acetate (13a) (90%), 17β-nitroamino-5α-androstan-3β-yl acetate (14a) (75%), 12β-nitroamino-(25*R*)-5α-spirostan-3β-yl acetate (15a) (65%),† and 23*R*-nitroamino-(20*S*,22*S*,25*S*)-5β-spirostan-3β-yl acetate (16) (95%).

The nitro-amine (13a) shows i.r. bands [8] at 3 370 and 3 240 (NH) and 1 580 cm^{-1} (NO_2); in its n.m.r. spectrum the amine proton and the 20-H are observed as multiplets at δ 9.2 and 4.2, respectively. The presence of the nitro-amine group can be confirmed by its mass spectrum, where fragments corresponding to $M^+ - NO_2$ and $M^+ - NH_2NO_2$ are observed. The

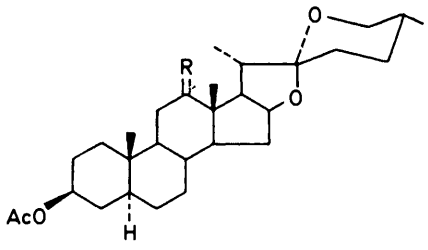
† The 12α-axial isomeric nitro-amine (15b) [δ 4.42 (m, $W_{\frac{1}{2}}$ 10 Hz, 12β-H)] is also formed in 16% yield.



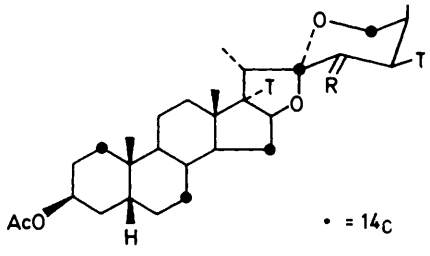
(1) R = O, R′ = OAc
(2) R = NOH, R′ = OAc
(3) R = NNO_2, R′ = OAc
(13a) R = α-H, β-$NHNO_2$, R′ = OAc
(13b) R = α-H, β-$NHNO_2$, R′ = OH



(4) R = O, R′ = OAc
(5) R = NOH, R′ = OAc
(6) R = NNO_2, R′ = OAc
(14a) R = α-H, β-$NHNO_2$, R′ = OAc
(14b) R = α-H, β-$NHNO_2$, R′ = OH



(7) R = O
(8) R = NOH
(9) R = NNO_2
(15a) R = α-H, β-$NHNO_2$
(15b) R = β-H, α-$NHNO_2$



• = ^{14}C

(10) R = H_2
(11) R = O
(12) R = NNO_2

Scheme 2

C-20 stereochemistry in (13a) was assumed to be *R* * by analogy with 20β-alcohols obtained almost exclusively by sodium borohydride reduction of 20-oxopregnanes.[10] The structures of the other steroidal nitro-amines (14a), (15a), and (16) were established in a similar way. The β-configuration of the nitro-amine group in (14a) and (15a) was determined by the shape of the signal corresponding to the geminal protons in their n.m.r. spectra which appear, after exchange of the amine protons with deuterium oxide, as a triplet at δ 4.05 (*J* 6 Hz) and a broad multiplet at 4.0 ($W_{\frac{1}{2}}$ 24 Hz), respectively. The same forms of the signals are observed in the n.m.r. spectra of 17β- and 12β-hydroxy-steroids.[12] The 23α-H signal in the n.m.r. spectrum of (16) could be observed without overlapping with C-3 and C-16 protons, using a 240 MHz apparatus; this appears, after irradiation of the amine proton, as a narrow multiplet at δ 4.27 ($W_{\frac{1}{2}}$ 14 Hz) as expected for the 23-axial configuration of the nitro-amine group.

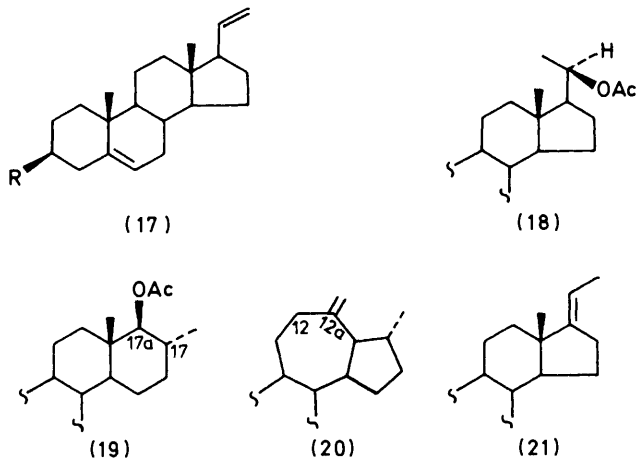
Denitroamination Reactions.—The denitroaminations were accomplished, at room temperature, by treatment of the nitro-amines with acetic anhydride and pyridine for 12 h. Nitrogen-bearing compounds were not isolated from these reactions. The observed products can be conveniently explained by an ion pair mechanism as shown in Scheme 1.

The 20β-nitro-amine (13a) yielded under these conditions the olefin (17) (26%) [13] produced by β-hydrogen-elimination,† the 20β-acetate (18) (16%) [15] coming from substitution by the counter ion with total retention of configuration, and the Wagner-Meerwein rearranged compounds (19) (22%) [16] and (20) (6%). The rearrangement that produces the D-homo-compounds (uranediol rearrangement) is common in the heterolysis of other 20β-steroid derivatives [4b,5] due to the highly favourable conformational situation [17] of the side chain in these substances. The structure of the C-homo-compound (20) is tentatively assigned by spectroscopic data; from its high-resolution mass spectrum a $C_{23}H_{34}O_2$ molecular formula can be deduced, and the principal fragments agree with this structure. The presence of an exocyclic double bond can be deduced by i.r. absorptions at 3 090 and 890 cm^{-1} and by two broad singlets at δ 4.89 and 4.70 in the n.m.r. spectrum. The methyl groups are observed at δ 1.14 (s, 10-Me) and 0.99 (d, *J* 7 Hz, 17-Me). This compound (20) probably arose from migration of the C(16)–C(17) bond to C-20 and formation of the carbonium ion (23) (Scheme 4) which can be stabilized by addition of acetate anion (path a) to give (19) or by migration of the C(13)–C(14) bond and loss of a hydrogen from C-18 to give (20) (path b). A carbonium ion like (24) has been postulated by Hirschmann [4a] as an intermediate during the formolysis of 20β-tosyloxypregnane to explain the formation of epimeric compounds at C-13, C-17, and C-17a during the uranediol rearrangement.

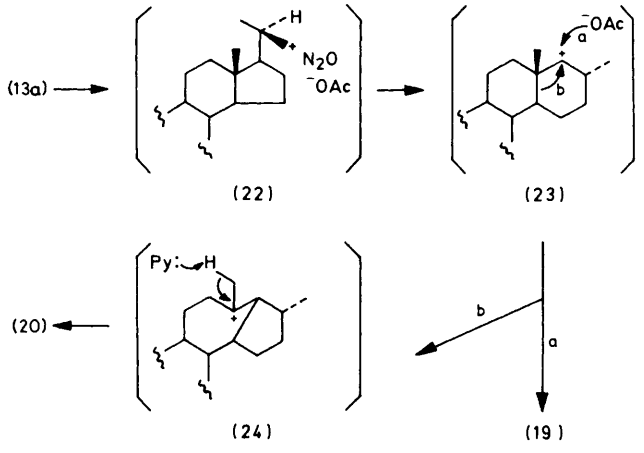
In our case, the absence of epimers of (19) indicates that the carbonium ion (24) is preferentially base stabilized by the loss of a C-18 hydrogen to give (20). During the nitrous acid deamination the 20β-aminopregnane behaves differently from the 20β-nitro-amine (13a) giving, almost exclusively, transposition products of the D-homo-androstane type; no substitution products such as compound (18) were observed.[3b]

* To confirm its 20*R*-stereochemistry, the 20*S*-isomer of (13b) [m.p. 238—240 °C (acetone–n-hexane), δ ([$^2H_5$]pyridine) 0.71 (13-Me), 1.03 (10-Me), and 1.35 (20-Me)] was synthesized by nitration [11] with ethyl nitrate of the lithium salt of 20*S*-aminopregn-5-en-3β-ol.[10b]

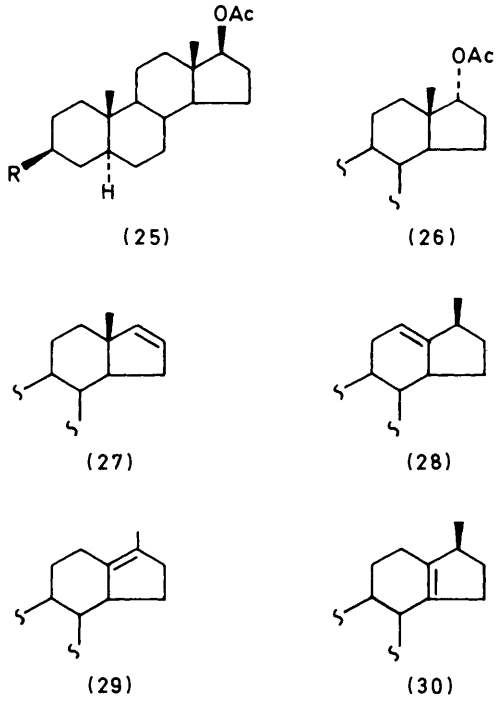
† In one case a small amount of isomerized *E*-olefin (21) [14] was obtained (1.5%).



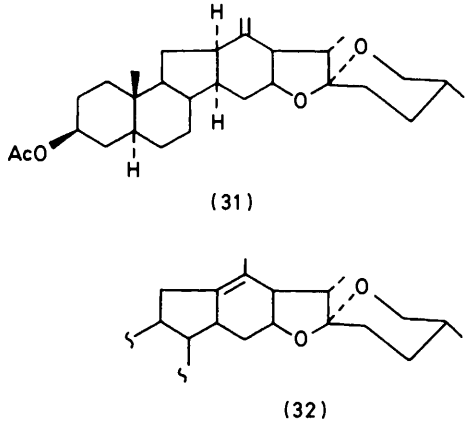
Scheme 3



Scheme 4



Scheme 5



Scheme 6

Three types of reaction are involved in the denitroamination of the 17β-nitro-amine (14a): (i) substitution is the predominant path (46%), products (25a) and (26a) being obtained with 65% of invertion of configuration at C-17; (ii) a β-elimination reaction to give the olefin (27a) (13%); and (iii) the 1,2-methyl-shift rearranged compounds (28a) (9%), (29a) (10%), and (30a) (10%). The n.m.r. spectrum of the previously undescribed olefin (28a) shows an angular methyl group at δ 0.79, a methyl doublet at δ 1.00 (*J* 7 Hz), and a vinyl proton at δ 5.3. The rearranged olefins (28a), (29a), and (30a) are the expected products from a C-17 carbonium ion, *e.g.* the solvolysis of 17β-tosylates,[18] the acid-catalyzed dehydration of the 17β-alcohols,[6] and the elimination of a 17β-benzamide.[19] In all these reactions a mixture of olefins was obtained containing the $\Delta^{13(17)}$ isomer as the main product, with lesser amounts of Δ^{13} and other isomeric olefins. The olefin (27a), which has not been detected in the aforementioned reactions, probably arose through a β-elimination *via* an ion pair mechanism. In contrast with the denitroamination reaction, the nitrous acid deamination of 17β-amines [3c] gave the 17β-alcohol exclusively and quantitatively with total retention of configuration.

The denitroamination of the 12β-nitro-amine (15a) affords almost quantitatively the rearranged C-nor-D-homo-compounds (31) (95%) and (32) (5%). The high yield of the kinetic exocyclic olefin is in agreement [3a] with the decomposition of the 12β-tosylate of rockogenin acetate in refluxing pyridine (*exo* : *endo* 90 : 10) and in contrast with the nitrous acid deamination of 12β-amines (*exo* : *endo* 22 : 78).*

The reaction of the 23*R*-nitro-amine (16) with acetic anhydride and pyridine gave the 23-dehydrosarsasapogenin acetate (34) in 95% yield; no substitution products are formed in agreement with the axial configuration of the nitro-amine.[1] This olefin (34) has been previously obtained by pyrolytic elimination of the 23*S*-phenylselenoxide of sarsasapogenin acetate.[20] We have reported [20] that the sarsa-

* In the solvolysis of different 12β-substituted steroids [3a] the ratio *exo* to *endo* olefins has been reported to be highly dependent on the solvent and the reaction conditions.

Table. ^{1}H N.m.r. data (δ in $CDCl_3$) (*J*/Hz or $W_{\frac{1}{2}}$/Hz in parentheses)

Compd.	3-H	6-H	17-H	20-H	10-Me	13-Me	20-Me	OAc	NH
(3)	4.6 (m, 20)	5.38 (m, 10)			1.02 (s)	0.75 (s)	2.02 (s)	2.02 (s)	
(13a)	4.6 (m)	5.38 (m, 10)		4.2 (m)	1.01 (s)	0.71 (s)	1.18 (d, 6)	2.04 (s)	9.2 (m, 18)
(17)	4.7 (m, 20)	5.42 (m, 12)		5.8 (m, 36)	1.04 (s)	0.61 (s)	5.07, 4.91 [a] (br s, m)		
(18)	4.6 (m)	5.39 (m, 12)		4.85 (m)	1.02 (s)	0.65 (s)	1.16 (d, 7)	2.02 (s)	
(19)	4.6 (m)	5.37 (m, 12)	4.36 [b] (d, 11)		0.98 (s)	0.85 (s)	0.78 [c] (d, 6)	2.00, 2.04 (s)	
(20)	4.6 (m)	5.37 (m, 12)			1.14 (s)	4.89, 4.70 [d] (br s)	0.99 (d, 7)	2.02 (s)	
(21)	4.6 (m, 20)	5.40 .(m, 12)		5.1 (m, 20)	1.04 (s)	0.76 (s)	1.55 (br d, 7)	2.02 (s)	
(6)	4.7 (m, 20)				1.02 (s)	0.86 (s)		2.01 (s)	
(14a)	4.7 (m, 20)		4.05 (m, 20)		0.83 (s)	0.75 (s)		2.01 (s)	8.8 (m, 13)

Compd.	3-H	12-H	16-H	23-H	26-H	10-Me	13-Me	20-Me	OAc	NH
(27a)	4.7 (m, 20)		5.8 [e] (m, 27)			0.77 (s)	0.88 (s)		2.03 (s)	
(28a)	4.7 (m, 20)	5.3 (m, 9)				0.79 (s)	1.0 [f] (d, 7)		2.03 (s)	
(9)	4.7 (m, 20)		4.45 (m, 18)		3.43 (m, 15)	0.88 (s)	1.10 (s)	1.05 (d, 6)	1.98 (s)	
(15a)	4.65 (m, 20)	4.0 (m, 24)	4.45 (m, 18)		3.43 (m, 18)	0.85 (s)	0.78 (s)	0.91 (d, 6)	2.00 (s)	8.8 (m, 18)
(15b)	4.7 (m, 20)	4.42 (m, 10)	4.4 (m)		3.42 (m, 18)	0.85 (s)	0.94 (s)	0.95 (d, 6)	2.07 (s)	9.75 (m, 18)
(31)	4.7 (m)		4.1 (m)		3.5 (m, 15)	0.81 (s)	4.84 [g] (m, 9)	1.09 (d, 7)	2.02 (s)	
(32)	4.7 (m, 24)		4.15 (m, 20)		3.53 (m, 12)	0.77 (s)	1.64 (br s)	1.12 (d, 7)	2.01 (s)	
(12)	5.06 (m, 10)		4.56 (m, 22)		4.13, 3.38 (ABX, 12)	1.00 (s)	0.82 (s)	1.07 (d, 6)	2.04 (s)	
(16)	5.06 (m, 10)		4.44 (m, 24)	4.27 (m, 18)	4.09, 3.39 (ABX, 12)	0.99 (s)	0.79 (s)	1.08 (d, 7)	2.05 (s)	8.41 (m, 16)
(34)	5.10 (m, 10)		4.55 (m, 22)	6.04, 5.54 [h] (ABX, 10)	4.07, 3.48 (ABX, 11)	1.00 (s)	0.81 (s)	1.07 (d, 7)	2.04 (s)	

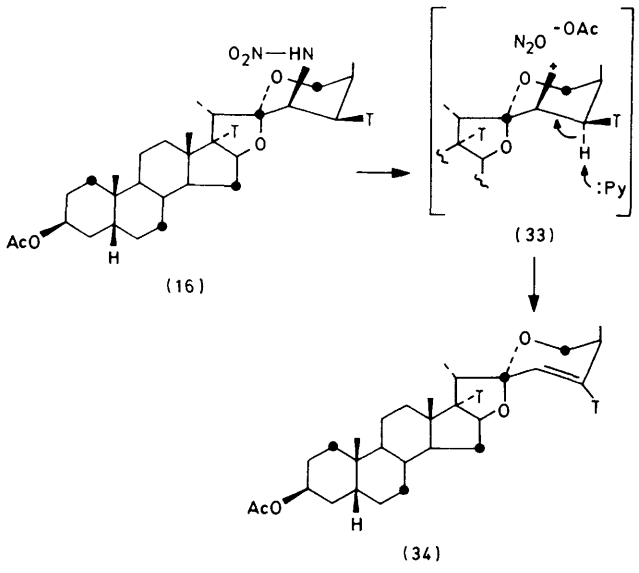
[a] 20- $=CH_2$. [b] 17aα-H. [c] 17-Me. [d] 12a- $=CH_2$. [e] 16-H and 17-H. [f] 17β-Me. [g] 13- $=CH_2$. [h] 24-H and 23-H.

sapogenin, biosynthesized by *Agave attenuata* Solm (Agavaceae) from [2-^{14}C, (4*R*)-4-^{3}H]mevalonic acid, has a β-equatorial tritium atom at C-24; this allowed us to study the stereochemistry of this β-hydrogen elimination. So, the labelled 23*R*-nitroaminosarsasapogenin acetate (16) (specific activity 1.63×10^5 d.p.m. mmol^{-1} of ^{14}C, and atomic ratio ^{3}H/^{14}C 2.01/5) was denitroaminated to give the olefin (34) (specific activity 1.60×10^5 d.p.m. mmol^{-1} of ^{14}C, atomic ratio ^{3}H/^{14}C 1.95/5) in which the ^{3}H-C_{24} remains. Hence, we conclude that the denitroamination reaction of the axial 23-nitro-amine (16) is mainly a solvent-induced *trans*-elimination as shown in (33). Similar results have been obtained for the deamination of primary amines in basic solvents.[21]

Experimental

M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured for solutions in $CHCl_3$. I.r. spectra were taken on a Perkin-Elmer 257 instrument. ^{1}H N.m.r. spectra were recorded with a Perkin-Elmer R-12B (60 MHz), Perkin-Elmer R-32 (90 MHz) or I.E.F. (240 MHz) instruments and ^{13}C n.m.r. spectra on a Varian C.F.T.-20 (20 MHz) instrument for solutions in $CDCl_3$ with Me_4Si as internal reference. Low- and high-resolution mass spectra were determined with a VG Micromass ZAB-2F spectrometer. ^{14}C and ^{3}H Labelled compounds were measured in a liquid scintillation counter Nuclear Chicago Isocap-300. T.l.c. was run on Merck silica gel 60, and column chromatography on Merck silica gel 0.063—0.2 mm. The spray reagent for t.l.c. was H_2SO_4–AcOH–H_2O (1 : 20 : 4) or vanillin (1 g)–H_2SO_4 (160 ml)–EtOH (40 ml).

20-Nitroiminopregn-5-en-3β-yl Acetate (3).—To a solution of 20-oxopregn-5-en-3β-yl acetate (1) (1 g) in dry pyridine (10 ml), hydroxylamine hydrochloride (0.5 g) was added, and the mixture was stirred at 60 °C for 3 h. After addition of water the mixture was extracted with ethyl acetate and the organic solution was washed with aqueous hydrochloric acid



Scheme 7

(10%), saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated under reduced pressure, to give the oxime (2) (0.98 g), which was used without purification in the next reaction. To the oxime (2) (0.72 g), dissolved in methylene chloride (34 ml) containing sodium nitrite (0.82 g), a mixture of acetic acid (1.2 ml) and methylene chloride (70 ml) was added dropwise at room temperature during 5 h. The mixture was then poured into water and extracted with diethyl ether. Work-up and column chromatography (benzene–ethyl acetate 99 : 1 as eluant) gave 20-*nitroiminopregn-5-en*-3β-*yl acetate* (3) (0.6 g), which crystallized from acetone–n-hexane, m.p. 175—176 °C, $[\alpha]_D$ −21° (*c* 0.23) (Found: C, 68.4; H, 8.5; N, 6.8. $C_{23}H_{34}N_2O_4$ requires C, 68.6; H, 8.5; N, 6.95%); *m/z* 342 (2%, M^+ − AcOH), 327 (1%), 296 (2%, M^+ − AcOH − NO_2), 282 (3%), 255 (8%), and 145 (100%); $\nu_{max.}$ (KBr) 1 725, 1 620, 1 580, and 1 315 cm^{-1}; δ_C 176.6 (20-C), 170.4 (O-*C*O-CH_3), 139.7 (5-C), 122.2 (6-C), 73.8 (3-C), 57.7 (17-C), 56.9 (14-C), 49.9 (9-C), 45.1 (13-C), 38.7 (16-C), 38.1 (4-C), 37.0 (1-C), 36.6 (10-C), 32.0 (8-C), 31.6 (7-C), 27.7 (2-C), 24.2 (15-C), 23.5 (12-C), 21.4 (O-CO-*C*H_3), 21.0 (11-C), 19.9 (21-C), 19.3 (19-C), and 13.1 (18-C).

17-*Nitroimino*-5α-*androstan*-3β-*yl Acetate* (6).—A solution of 17-oxo-5α-androstan-3β-yl acetate (4) (2.5 g) and hydroxylamine hydrochloride (1 g) in pyridine (40 ml) was treated as indicated for 20-oxopreg-5-en-3β-yl acetate (1), to yield the oxime (5) (2.4 g) [$\nu_{max.}$ ($CHCl_3$) 3 560 and 1 715 cm^{-1}] which was used without purification in the next reaction. To a solution of the oxime (2.4 g) in methylene chloride (50 ml) and acetic acid (6 ml), solid sodium nitrite (2.5 g) was added at room temperature for 1 h. Work-up and column chromatography (benzene–n-hexane 75 : 25) yielded the starting ketone (4) (1.5 g) and 17-*nitroimino*-5α-*androstan*-3β-*yl acetate* (6) (0.68 g), m.p. 177—178 °C (n-hexane), $[\alpha]_D$ +5° (*c* 0.14) (Found: C, 67.2; H, 8.75; N, 7.7. $C_{21}H_{32}N_2O_4$ requires C, 67.0; H, 8.6; N, 7.45%); *m/z* 376 (70%, M^+), 360 (15%), 345 (10%), 343 (15%), 330 (20%, M^+ − NO_2), 316 (20%, M^+ − AcOH), and 270 (100%, M^+ − NO_2 − AcOH); $\nu_{max.}$ ($CHCl_3$) 1 715, 1 640, and 1 560 cm^{-1}.

12-*Nitroimino*-(25R)-5α-*spirostan*-3β-*yl Acetate* (9).—A solution of 12-oxo-(25*R*)-5α-spirostan-3β-yl acetate (7) (2.5 g) and hydroxylamine hydrochloride (1 g) in pyridine (40 ml) was treated as indicated for the preparation of (2), to afford the oxime (8) (2.5 g) [$\nu_{max.}$ ($CHCl_3$) 3 580 and 1 715 cm^{-1}]. The nitro-imine (9) was prepared in quantitative yield from this oxime (8), as previously described for (6). 12-*Nitroimino*-(25R)-5α-*spirostan*-3β-*yl acetate* (9) crystallized from n-hexane, m.p. 197—198 °C, $[\alpha]_D$ +12° (*c* 0.25) (Found: C, 67.25; H, 8.75; N, 5.45. $C_{29}H_{44}N_2O_6$ requires C, 67.4; H, 8.6; N, 5.4%); *m/z* 470 (50%, M^+ − NO_2), 356 (15%), 256 (15%), and 139 (100%); $\nu_{max.}$ ($CHCl_3$) 1 720, 1 620, and 1 560 cm^{-1}.

23-*Nitroimino*-(20S,22S,25S)-5β-*spirostan*-3β-*yl Acetate* (12).—Sarsapogenin acetate (10), biosynthesized by an *Agave attenuata* Solm. culture [20] with [2-^{14}C, (4*R*)-4-^{3}H]-mevalonic acid (43 mg, 6.88 × 10^5 d.p.m. $mmol^{-1}$ of ^{14}C) was diluted with carrier material and crystallized to constant specific activity: 1.64 × 10^5 d.p.m. $mmol^{-1}$ of ^{14}C and atomic ratio ^{3}H/^{14}C 2.08/5. To a solution of this material (199 mg) in acetic acid (5 ml) and boron trifluoride–diethyl ether complex (0.2 ml), sodium nitrite (150 mg) was added in small portions with stirring at room temperature during 1.5 h. The mixture was then poured into water, extracted with chloroform and washed with aqueous $NaHCO_3$ and water. After drying over Na_2SO_4 the solvent was evaporated and the residue chromatographed (benzene as eluant) to afford 23-oxo-(20*S*,22*S*,25*S*)-5β-spirostan-3β-yl acetate (11) (30 mg), $\nu_{max.}$ (KBr) 1 740 cm^{-1} and 23-*nitroimino*-(20S,22S,25S)-5β-*spirostan*-3β-*yl acetate* (12) (113 mg), m.p. 173—175 °C (MeOH), $[\alpha]_D$ −74° (*c* 0.19) (Found: C, 67.3; H, 8.6; N, 5.4. $C_{29}H_{44}N_2O_6$ requires C, 67.4; H, 8.6; N, 5.4%); *m/z* 516 (0.2%, M^+), 470 (33%, M^+ − NO_2), 456 (4%, M^+ − AcOH), 410 (32%, M^+ − NO_2 − AcOH), 389 (3%), 344 (22%), 329 (33%), 315 (19%), 284 (27%), and 255 (100%); $\nu_{max.}$ ($CHCl_3$) 1 735, 1 644, 1 575, and 1 318 cm^{-1}.

Sodium Borohydride Reduction of Steroid Nitro-amines: General Procedure.—To a solution of the steroid nitro-imine (1 mmol) in absolute ethanol (50 ml), sodium borohydride (9 mmol) was added and the mixture was stirred at ambient temperature for 1.5 h. After the addition of water the mixture was acidified with aqueous hydrochloric acid (10%) and extracted with chloroform. The organic layer was washed with aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated under reduced pressure.

(i) 20β-*Nitroaminopregn-5-en*-3β-*yl acetate* (13a). This was purified by column chromatography (benzene–ethyl acetate 9 : 1) to give a 90% yield, m.p. 189—190 °C (acetone–n-hexane), $[\alpha]_D$ −56° (*c* 0.22) (Found: C, 68.35; H, 9.0; N, 6.85. $C_{23}H_{36}N_2O_4$ requires C, 68.3; H, 9.0; N, 6.9%); *m/z* 344 (100%, M^+ − AcOH), 329 (10%), 298 (30%, M^+ − AcOH − NO_2), 282 (35%, M^+ − AcOH − NH_2NO_2), and 267 (25%); $\nu_{max.}$ ($CHCl_3$) 3 370, 3 240, 1 720, and 1 580 cm^{-1}; δ_C 171.4 (O-*C*O-CH_3), 139.8 (5-C), 122.3 (6-C), 74.2 (3-C), 55.9 (14-C), 54.4 (20-C), 53.5 (17-C), 50.0 (9-C), 42.2 (13-C), 38.9 (16-C), 38.0 (4-C), 37.1 (1-C), 36.6 (10-C), 31.8 (7-C), 31.8 (8-C), 27.7 (2-C), 26.7 (12-C), 24.1 (15-C), 21.4 (O-CO-*C*H_3), 20.9 (11-C), 19.2 (19-C), 18.7 (21-C), and 12.4 (18-C). Saponification with 2% potassium hydroxide in methanol gave the alcohol (13b), which crystallized from acetone–n-hexane, m.p. 244—246 °C (Found: C, 69.5; H, 9.4; N, 7.6. $C_{21}H_{34}N_2O_3$ requires C, 69.6; H, 9.45; N, 7.75%); *m/z* 362 (74%, M^+), 344 (71%, M^+ − H_2O), 316 (21%, M^+ − NO_2), 300 (100%, M^+ − NH_2NO_2), 285 (76%), and 267 (99%); $\nu_{max.}$ (KBr) 3 380, 3 180, and 1 580 cm^{-1}; δ([$^2H_5$]pyridine) 5.4 (1 H, m, $W_{\frac{1}{2}}$ 10 Hz, 6-H), 4.4 (1 H, m, $W_{\frac{1}{2}}$ 24 Hz, 20-H), 3.7 (1 H, m, $W_{\frac{1}{2}}$ 30 Hz, 3α-H), 1.21 (3 H, d, *J* 7 Hz, 20-Me), 1.02 (3 H, s, 10-Me), and 0.74 (3 H, s, 13-Me).

(ii) 17β-*Nitroamino*-5α-*androstan*-3β-*yl acetate* (14a). This was purified by crystallization from ethyl acetate–n-hexane to give a 75% yield, m.p. 158—159 °C, $[\alpha]_D$ =0° (*c* 0.20) (Found: C, 66.9; H, 9.15; N, 7.3. $C_{21}H_{34}N_2O_4$ requires C, 66.65; H, 9.05; N, 7.4%); *m/z* 332 (8%, $M^+ - NO_2$), 318 (6%, M^+ −AcOH), 316 (8%, $M^+ - NH_2NO_2$), 301 (3%), 272 (12%, M^+ −AcOH − NO_2), 256 (10%, M^+ −AcOH − NH_2NO_2), 241 (20%), and 148 (100%); $\nu_{max.}$ ($CHCl_3$) 3 390, 1 720, and 1 575 cm^{-1}; δ 4.05 (1 H, m, $W_{\frac{1}{2}}$ 20 Hz, 17α-H; $+D_2O$: t, *J* 6 Hz).

(iii) 12β-*Nitroamino*-(25R)-5α-*spirostan*-3β-*yl acetate* (15a) *and* 12α-*nitroamino*-(25R)-5α-*spirostan*-3β-*yl acetate* (15b). A mixture of the two stereoisomers at C-12 was obtained by reduction of the 12-nitro-imine (9) which was chromatographed (benzene–ethyl acetate 97 : 3) to yield (15a) (65%) and (15b) (15%). The 12β-*nitro-amine* (15a) had m.p. 238—240 °C (n-hexane), $[\alpha]_D$ −42° (*c* 0.10) (Found: C, 67.0; H, 9.3; N, 5.55. $C_{29}H_{46}N_2O_6$ requires C, 67.15; H, 8.95; N, 5.4%); *m/z* 518 (2%, M^+), 472 (3%, $M^+ - NO_2$), 456 (5%, $M^+ - NH_2NO_2$), 446 (5%), 358 (4%), and 139 (100%); $\nu_{max.}$ ($CHCl_3$) 3 370, 1 710, and 1 570 cm^{-1}. The 12α-*nitro-amine* (15b) crystallized from n-hexane, m.p. 234—236 °C, $[\alpha]_D$ −11° (*c* 0.10) (Found: C, 67.4; H, 9.2; N, 5.6. $C_{29}H_{46}N_2O_6$ requires C, 67.15; H, 8.95; N, 5.4%); *m/z* 472 (2%, $M^+ - NO_2$), 456 (1%, $M^+ - NH_2NO_2$), 446 (1%), 358 (12%), and 139 (100%); $\nu_{max.}$ ($CHCl_3$) 3 380, 3 220, 1 710, and 1 575 cm^{-1}.

(iv) 23R-*Nitroamino*-(20S,22S,25S)-5β-*spirostan*-3β-*yl acetate* (16). This was purified by column chromatography (benzene–ethyl acetate 93 : 7) to give a 95% yield and crystallized from methanol to its constant specific activity: 1.63 × 10^5 d.p.m. $mmol^{-1}$ of ^{14}C and atomic ratio $^3H/^{14}C$ 2.01/5; m.p. 177—179 °C, $[\alpha]_D$ −83° (*c* 0.34) (Found: C, 66.95; H, 8.9; N, 5.55. $C_{29}H_{46}N_2O_6$ requires C, 67.15; H, 8.95; N, 5.4%); *m/z* 472 (15%, $M^+ - NO_2$), 456 (85%, $M^+ - NH_2NO_2$), 396 (3%, M^+ −AcOH − NH_2NO_2), 255 (55%), and 137 (100%); $\nu_{max.}$ (KBr) 3 400, 1 735, and 1 580 cm^{-1}; δ(240 MHz) 4.27 (1 H, m, $W_{\frac{1}{2}}$ 18 Hz, upon irradiation at 8.41, $W_{\frac{1}{2}}$ 14 Hz, 23α-H).

Denitroamination of Steroid Nitro-amines: General Procedure.—To a solution of the steroid nitro-amine (1 mmol) in pyridine (30 ml), acetic anhydride (6 ml) was added and the mixture was kept at room temperature overnight. After addition of ice–water and solid sodium hydrogen carbonate, the products were extracted with diethyl ether. The organic layer was washed with aqueous hydrochloric acid, aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated under reduced pressure.

(i) *Reaction of* 20β-*nitroaminopreg*-5-*en*-3β-*yl acetate* (13a). The nitro-amine (13a) (1 g) gave a mixture which was chromatographed on silica gel (benzene–ethyl acetate, 98 : 2) and silica gel containing 20% $AgNO_3$ (benzene–n-hexane, 7 : 3) to give pregna-5,20-dien-3β-yl acetate (17) (0.22 g), pregn-5-en-3β,20β-diyl diacetate (18) (0.16 g), 17α-methyl-D-homo-androst-5-en-3,17aβ-diyl diacetate (19) (0.22 g), 17α-*methyl*-12a-*methylene*-C(12a)-*homo*-18-*norandrost*-5-*en*-3β-*yl acetate* (20) (0.05 g), and pregna-5,17(20)*E*-dien-3β-yl acetate (21) (0.012 g).

Compound (17) had m.p. 132—135 °C (MeOH), $[\alpha]_D$ −82° (*c* 0.29) (lit.,[13] m.p. 132.5—135 °C, $[\alpha]_D$ −77°); *m/z* 282.2336 (52%, M^+ −AcOH, $C_{21}H_{30}$, 282.2347), 267.2090 (17%, $C_{20}H_{20}$, 267.2113), and 213.1638 (16%, $C_{16}H_{21}$, 213.1643); $\nu_{max.}$ (KBr) 3 080 and 1 725 cm^{-1}. Compound (18), crystallized from methanol, had m.p. 130—131 °C, $[\alpha]_D$ −36° (*c* 0.20) (lit.,[15] m.p. 128.5—131 °C, $[\alpha]_D$ −34 ± 4°); *m/z* 342 (100%, M^+ −AcOH) and 282 (15%, M^+ −2 AcOH); $\nu_{max.}$ (KBr) 1 730 cm^{-1} (Found: C, 74.4; H, 9.6. Calc. for $C_{25}H_{38}O_4$: C, 74.6; H, 9.5%). Compound (19) had m.p. 211—212 °C (MeOH), $[\alpha]_D$ −117° (*c* 0.3) (lit.,[16] m.p. 210—211 °C, $[\alpha]_D$ −112°); *m/z* 342 (100%, M^+ −AcOH) and 282 (3%, M^+ −2 AcOH); $\nu_{max.}$ (KBr) 1 730 cm^{-1} (Found: C, 74.7; H, 9.4. Calc. for $C_{25}H_{38}O_4$: C, 74.6; H, 9.5%). Compound (21) crystallized from methanol had m.p. 142—145 °C, $[\alpha]_D$ −68° (*c* 0.24) (lit.,[14] m.p. 143—143.5 °C, $[\alpha]_D$ −72°); *m/z* 282 (100%, M^+ −AcOH) (Found: C, 80.75; H, 9.9. Calc. for $C_{23}H_{34}O_2$: C, 80.65; H, 10.0%). Compound (20) had m.p. 127—130 °C (MeOH), $[\alpha]_D$ −67° (*c* 0.27); *m/z* 282.2330 (M^+ −AcOH, $C_{21}H_{30}$ requires 282.2347), 200.1542 ($C_{15}H_{20}$ requires 200.1565), and 81.0692 (C_6H_9 requires 81.0704); $\nu_{max.}$ (KBr) 3 090 and 1 735 cm^{-1}.

(ii) *Reaction of* 17β-*nitroamino*-5α-*androstan*-3β-*yl acetate* (14a). Chromatography on silica gel (benzene) and silica gel containing 20% $AgNO_3$ (n-hexane–ethyl acetate 99 : 1) of the crude product of the denitroamination reaction of (14a) (3.1 g) yielded an unresolved mixture (1.4 g) of 5α-androstan-3β,17β-diyl diacetate (25a) and 5α-androstan-3β,17α-diyl diacetate (26a) in a ratio 1 : 2 (as estimated by ^1H n.m.r.), 5α-androst-16-en-3β-yl acetate (27a) (0.41 g), 17β-methyl-18-nor-5α-androst-12-en-3β-yl acetate (28a) (0.23 g), and a mixture (0.55 g) of 17-methyl-18-nor-5α-androst-13(17)-en-3β-yl acetate (29a) and 17β-methyl-18-nor-5α-androst-13-en-3β-yl acetate (30a). The mixture of (25a) and (26a)—or their hydrolysis derivatives—which could not be resolved by t.l.c. or g.l.c., had n.m.r.[12] signals at δ 4.80 (d, *J* 7 Hz, 17β-H), 4.6 (m, 3α-H and 17α-H), 0.83 (s, 10-Me), 0.78 [s, 13 Me in (25a)], and 0.74 [s, 13-Me in (26a)]; *m/z* 316 (62%, M^+ −AcOH). Compound (27a) crystallized from methanol, m.p. 66—67 °C, $[\alpha]_D$ −3° (*c* 0.20); *m/z* 316 (63%, M^+), 301 (38%, M^+ −Me), 256 (23%, M^+ −AcOH), and 241 (100%, M^+ −AcOH − Me) (Found: C, 79.5; H, 10.05. $C_{21}H_{32}O_2$ requires C, 79.7; H, 10.2%). Saponification of (27a) with 2% potassium hydroxide in methanol yielded the alcohol (27b), m.p. 122—123 °C (MeOH), $[\alpha]_D$ +12° (*c* 0.24) (lit.,[22] m.p. 125—126 °C, $[\alpha]_D$ +14°). Compound (28a) was obtained as a gum, *m/z* 316 (12%, M^+), 256 (11%, M^+ −AcOH), and 241 (10%, M^+ −AcOH − Me). Saponification with 2% potassium hydroxide in methanol yielded the alcohol (28b), m.p. 88—89 °C (n-hexane), $[\alpha]_D$ +3° (*c* 0.25) (Found: C, 83.25; H, 10.9. $C_{19}H_{30}O$ requires C, 83.15; H, 11.0%); *m/z* 274 (52%, M^+), 259 (24%, M^+ −Me), 256 (6%, $M^+ - H_2O$), 241 (26%, $M^+ - H_2O$ − Me), and 148 (100%); δ 5.3 (1 H, m, $W_{\frac{1}{2}}$ 10 Hz, 12-H), 3.6 (1 H, m, $W_{\frac{1}{2}}$ 30 Hz, 3α-H), 1.00 (3 H, d, *J* 7 Hz, 17β-Me), and 0.79 (3 H, s, 10-Me). The mixture of tetrasubstituted olefins (29a) and (30a) which could not be resolved, by silica gel or silica gel-20% $AgNO_3$ t.l.c. or g.l.c. techniques, had *m/z* 316 (61%, M^+) and 256 (13%, M^+ −AcOH); δ[19] 1.60 [br s, 17-Me in (29a)], 0.95 [d, *J* 7 Hz, 17β-Me in (30a)], 0.80 [s, 10-Me in (30a)], and 0.75 [s, 10-Me in (29a)].

(iii) *Reaction of* 12β-*nitroamino*-(25R)-5α-*spirostan*-3β-*yl acetate* (15a). The nitro-amine (15a) (0.25 g) gave a residue which was chromatographed on a column of silica gel containing 20% $AgNO_3$ (benzene–n-hexane 3 : 2) to yield 14(13 → 12α*H*)*abeo*-(25R)-5α-spirost-13(18)-en-3β-yl acetate (31) (0.2 g), m.p. 227—228 °C (n-hexane), $[\alpha]_D$ −88° (*c* 0.12) (lit.,[23] m.p. 222—224 °C, $[\alpha]_D$ −80.6°) (Found: C, 76.3; H, 9.6. Calc. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7%); *m/z* 456 (4%, M^+), 438 (2%), 414 (2%), 384 (2%), 342 (5%), 165 (35%), 139 (25%), and 126 (100%); $\nu_{max.}$ (CS_2) 3 080, 1 720, and 1 640 cm^{-1}; and 14(13 → 12)*abeo*-(25*R*)-5α-spirost-12-en-3β-yl acetate (32) (0.01 g), m.p. 144—146 °C (MeOH), $[\alpha]_D$ −50° (*c* 0.18) (lit.,[23] m.p. 140—142 °C, $[\alpha]_D$ −56°) (Found: C, 76.4; H, 9.6. Calc. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7%); *m/z* 456 (9%, M^+), 438 (8%), 342 (30%), and 126 (100%).

(iv) *Reaction of* 23R-*nitroamino*-(20S,22S,25S)-5β-*spirostan*-

3β-*yl acetate* (16). The nitro-amine (16) (90 mg) yielded, after purification by column chromatography (benzene–ethyl acetate 95 : 5), (20*S*,22*R*,25*S*)-5β-spirost-23-en-3β-yl acetate (34) (75 mg) which was recrystallized from methanol to its constant specific activity 1.60×10^5 d.p.m. mmol^{-1} of ^{14}C and atomic ratio $^3H/^{14}C$ 1.95/5; m.p. 148—149 °C, $[\alpha]_D$ +7° (*c* 0.13) (lit.,[20] 147—148 °C, $[\alpha]_D$ +6°) (Found: C, 75.9; H, 9.75. Calc. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7%); *m*/*z* 456 (3%, M^+), 441 (1%, M^+ − Me), 284 (2%), 269 (2%), 255 (2%), 137 (100%), and 113 (25%); $\nu_{max.}$ 3 025 and 1 735 cm^{-1}; δ 6.12, 6.06, 6.02, and 5.95 (1 H, *A*BX, 24-H).

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