Steroidal *N*-Nitroamines. Part 4.[1] Intramolecular Functionalization of *N*-Nitroamine Radicals: Synthesis of 1,4-Nitroimine Compounds

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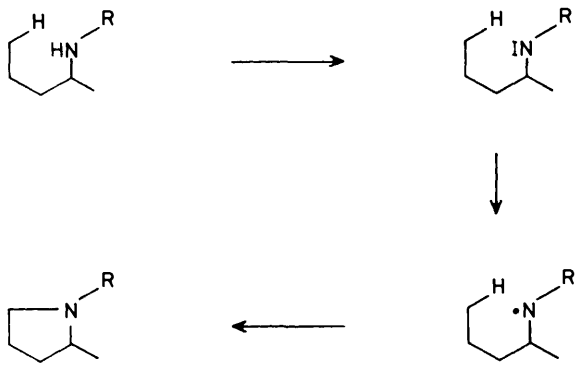
Photolysis of 6β-nitroamino-5α-cholestane (**4**), 6β-nitroamino-5α-cholestan-3β-yl acetate (**5**), 2β-nitroamino-5α-cholestane (**13**), 4β-nitroamino-5α-cholestane (**17**), (20*R*)-20-nitroaminopregn-5-en-3β-yl acetate (**26**), (20*R*)- (**31**) and (20*S*)- (**34**)-nitroamino-5α-pregnan-3β-yl acetate, (23*R*,25*S*)-3β-acetoxy-23-nitroamino-5β-spirostan (**46**), 3β-nitroaminofriedelane (**53**), and methyl 3β-nitroaminofriedelan-29-oate (**54**) in the presence of iodine and various oxidative reagents leads to neutral nitroaminyl radicals which undergo intramolecular hydrogen-abstraction to produce in most cases *N*-nitroimine compounds. Best results were obtained with the system iodine and (diacetoxyiodo)benzene.

The introduction of functional groups into non-activated skeletal positions in organic compounds is mostly performed by the known strategy of generating free radicals close to such centres. Intramolecular functionalizations due to alkoxy radicals have been exhaustively studied[2] but little attention has been devoted to those promoted by nitrogen radicals.[3] The sole reaction of this type with interest in the synthesis of cyclic amines is the Hofmann–Löffler–Freytag reaction, but its use is limited by the strongly acidic conditions needed to generate the required ammonium radical intermediates and which are not compatible with sensitive molecules. This difficulty has been overcome by the use of neutral aminyl radicals as we have reported recently.[4]

It occurred to us that a potential use in synthesis, particularly for the preparation of biologically important pyrrolidines, lay in the photolysis of *N*-iodoamide derivatives to give 1,4-epimine compounds (Scheme). The amine substituent should act to



Scheme.

stabilize the *N*-radical in order to promote the hydrogen abstraction. Exploitation of these features has led to the development of a synthetically useful procedure to obtain 1,4- and 1,5-epimine compounds by photolysis of *N*-iodonitroamines (R = NO_2),[4a] *N*-iodophosphoramidates R = $P(O)(OEt)_2$, $P(O)(OPh)_2$, and $P(O)(OCH_2Ph)_2$,[4b] and *N*-iodocyanamides (R = CN),[4c,d] generated *in situ* by reaction of the corresponding amine derivatives with iodine in the presence of an oxidative reagent.

In a preliminary communication[4a] we have shown that intramolecular functionalization of C-18 and C-19 steroidal methyl groups is also possible from conveniently situated *N*-nitroamines. We now report the synthesis of several steroidal and triterpenic *N*-nitroamines and the results of our study of the photolysis of the corresponding *N*-iodonitroamines.

Preparation of the Substrates.—6β-Nitroamino-5α-cholestan-3β-yl acetate (**5**),[5a] (20*R*)-20-nitroaminopregn-5-en-3β-yl acetate (**26**),[5b] and (23*R*,25*S*)-3β-acetoxy-23-nitroamino-5α-spirostan (**46**)[5b] have been described in previous papers of this series.

6β-Nitroamino-5α-cholestane (**4**), 2β-nitroamino-5β-nitroamino-5α-cholestane (**13**), 4β-nitroamino-5α-cholestane (**17**), 3β-nitroaminofriedelane (**53**), and methyl 3β-nitroaminofriedelan-29-oate (**54**) were prepared by sodium borohydride reduction of the corresponding unstable nitroimines (**3**), (**12**), (**16**), (**51**), and (**52**) obtained by nitrosation of the oximes (**2**), (**11**), (**15**), (**49**), and (**50**) with sodium nitrite in acetic acid–dichloromethane.[5b]

The starting cholestan-6- (**1**), -2- (**10**), and -4- (**14**)-ones were synthesized as follows: hydroboration and subsequent oxidation of cholest-5-ene gave cholestan-6-one (**1**). A mixture of the cholestan-2- and -4-was prepared by 1,2-carbonyl transposition of 5α-cholestan-3-one (**6**), following the procedure of Nakai and Mimura.[6] The vinyl sulphides (**18**) and (**19**), obtained after sulphenylation of the dianion of the 3-tosylhydrazone (**7**), followed by the Shapiro reaction, were, in our hands, reluctant to undergo hydrolysis by the method suggested by the authors.[7] Partial hydrolysis to ketones was achieved on heating the mixture at 80 °C for 4 days with 3 mol equiv. of mercury(II) chloride in aqueous dioxane. The cholestan-2- and -4-one mixture was separated by careful rotative chromatography on a Chromatotron.

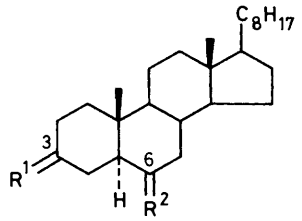
The synthesis of the 20*R*-(**31**) and 20*S*-(**34**) nitroamines in the pregnane series was performed starting from the corresponding amines obtained by reduction of the 20-oxime of 3β-hydroxypregn-5-en-20-one with sodium in propan-1-ol.[8] By this method a mixture (57:43) of the 20*R*-(**22**) and 20*S*-(**24**) amines was obtained, which was separated by chromatography. Both amines were treated subsequently with ethyl chloroformate and acetic anhydride to yield the acetyl carbamates (**23**) and (**25**).

Attempts to obtain *N*-nitrocarbamates[9] by nitration of carbamates (**23**) and (**25**) failed because nitration of the double bond occurs preferentially. To overcome this situation, the double bond was hydrogenated with H_2 and PtO_2 as catalyst. Treatment of the dihydro carbamates (**29**) and (**32**) with nitric acid in acetic anhydride gave the *N*-nitrocarbamates (**30**) and (**33**). Hydrolysis and decarboxylation of the *N*-nitrocarbamates to the required nitroamines (**31**) and (**34**) was achieved with ammonium hydroxide and dilute hydrochloric acid.

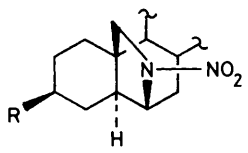
A more convenient method to obtain stereoselectively (20*S*)-20-amino-5α-pregnan-3β-yl acetate (**37**), and which avoids the tedious chromatographic separation of the 20*R* and 20*S* amines, is based on the reaction of 20-oxo-5α-pregnan-3β-yl acetate with (*S*)-(−)-1-phenylethylamine in the presence of toluene-*p*-sulphonic acid (PTSA), the obtained imine (**35**) being reduced with diborane to yield the benzylamine (**36**).[10] Removal of the benzyl group was realized by catalytic transfer hydrogenation with palladium-black and formic acid,[11] and the obtained amine (**37**) was treated as described above to give, through carbamate (**32**) and *N*-nitrocarbamate (**33**), the desired 20*S*-nitroamine (**34**).

Intramolecular Cyclization of N-*Nitroamines*.—The hydrogen-abstraction reaction was performed by photolysis of the *N*-nitroamines with visible light (2 × 150 W tungsten-filament lamps) in the presence of iodine and an oxidative reagent in cyclohexane or dichloromethane or mixtures of both under the conditions shown in the Table.

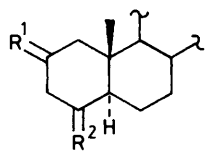
Photolysis of 6β-nitroaminocholestane (**4**) led to the 6β,19-



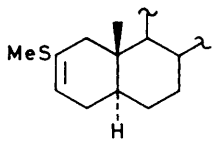
(**1**) $R^1 = H_2$, $R^2 = O$
(**2**) $R^1 = H_2$, $R^2 = NOH$
(**3**) $R^1 = H_2$, $R^2 = NNO_2$
(**4**) $R^1 = H_2$, $R^2 = \alpha\text{-}H, \beta\text{-}NHNO_2$
(**5**) $R^1 = \alpha\text{-}H, \beta\text{-}OAc, R^2 = \alpha\text{-}H, \beta\text{-}NHNO_2$
(**6**) $R^1 = O$, $R^2 = H_2$
(**7**) $R^1 = NNHTs$, $R^2 = H_2$



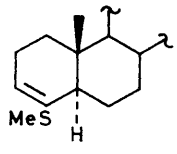
(**8**) R = H
(**9**) R = OAc



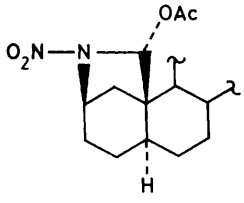
(**10**) $R^1 = O$, $R^2 = H_2$
(**11**) $R^1 = NOH$, $R^2 = H_2$
(**12**) $R^1 = NNO_2$, $R^2 = H_2$
(**13**) $R^1 = \alpha\text{-}H, \beta\text{-}NHNO_2$, $R^2 = H_2$
(**14**) $R^1 = H_2$, $R^2 = O$
(**15**) $R^1 = H_2$, $R^2 = NOH$
(**16**) $R^1 = H_2$, $R^2 = NNO_2$
(**17**) $R^1 = H_2$, $R^2 = \alpha\text{-}H, \beta\text{-}NHNO_2$



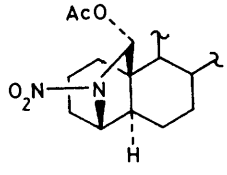
(**18**)



(**19**)



(**20**)



(**21**)

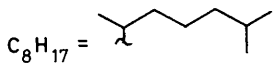
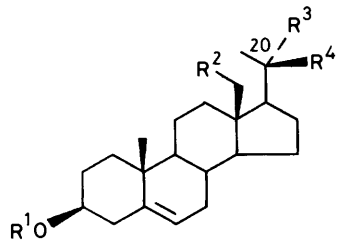


Table. Intramolecular cyclization of *N*-nitroamines[a]

Entry	*N*-Nitroamine	Reagent[b] (mmol)	Iodine (mmol)	Time (h)	Temp. (°C)	Solvent	Products (yield/%)
1	(**4**)	LTA (2.5)	1.5	2	80	Cy[d]	(**8**)(51)
2	(**4**)	HgO (4)	2.2	5	80	Cy	(**8**)(69)
3	(**4**)	$Hg(OAc)_2$ (2.5)	1.5	3	40—50	Cy	(**8**)(73)
4	(**4**)	DIB (1.5)	0.5	1.2	80	Cy	(**8**)(77)
5	(**4**)	DIB (1.5)	0.1	1.2	80	Cy	no reaction
6	(**4**)	PhIO (1.4)	0.5	5	80	Cy	(**8**)(trace)
7	(**5**)	LTA (5)	0.7	2	80	Cy	(**9**)(63)
8	(**5**)	HgO (22)	9	2	80	Cy	(**9**)(60)
9	(**13**)	LTA (2.4)	1.5	2	80	Cy	(**20**)(50)
10	(**13**)	DIB (2.4)	1.1	1.5	80	Cy	(**20**)(64)
11	(**17**)	LTA (2.4)	1.5	2	80	Cy	(**21**)(53),(**17**)(10)
12	(**26**)	HgO (3.7)	3.2	1.5	40—50	CH_2Cl_2	(**27**)(25)
13	(**26**)	DIB (1.5)	0.5	1.5	40—50	CH_2Cl_2	(**27**)(47)
14	(**31**)	HgO (3.8)	3.2	1.5	40—50	CH_2Cl_2	(**38**)(28)
15	(**34**)	HgO (3.7)	3	2.5	40	CH_2Cl_2	(**34**)(15),(**39**)(23),(**41**)(25)
16	(**34**)	DIB (1.5)	0.5	7	r.t.[c]	CH_2Cl_2	(**41**)(20),(**42**)(10),(**43**)(13),(**44**)(5)
17	(**46**)	LTA (4)	1.4	2	80	Cy	(**47**)(53),(**48**)(26)
18	(**53**)	LTA (3.2)	1.7	1	55—65	Cy-Cl_2CH_2	(**55**)(23),(**56**)(42)
19	(**54**)	LTA (3)	1.5	1.5	40—50	Cy-Cl_2CH_2	(**57**)(50),(**58**)(14)

[a] Under irradiation with two 150 W tungsten-filament lamps. [b] Per mmol of *N*-nitroamine. [c] Room temperature. [d] Cy = cyclohexane.



(22) $R^1 = R^2 = R^3 = H$, $R^4 = NH_2$

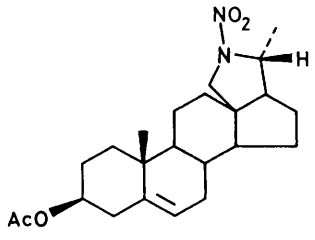
(23) $R^1 = Ac$, $R^2 = R^3 = H$, $R^4 = NHCO_2Et$

(24) $R^1 = R^2 = R^4 = H$, $R^3 = NH_2$

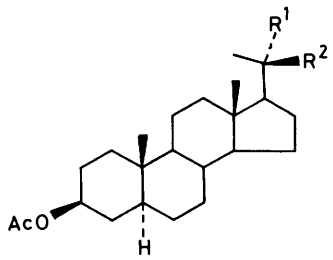
(25) $R^1 = Ac$, $R^2 = R^4 = H$, $R^3 = NHCO_2Et$

(26) $R^1 = Ac$, $R^2 = R^3 = H$, $R^4 = NHNO_2$

(27) $R^1 = Ac$, $R^2 = I$, $R^3 = H$, $R^4 = NHNO_2$



(28)



(29) $R^1 = H$, $R^2 = NHCO_2Et$

(30) $R^1 = H$, $R^2 = N(NO_2)CO_2Et$

(31) $R^1 = H$, $R^2 = NHNO_2$

(32) $R^1 = NHCO_2Et$, $R^2 = H$

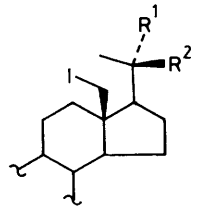
(33) $R^1 = N(NO_2)CO_2Et$, $R^2 = H$

(34) $R^1 = NHNO_2$, $R^2 = H$

(35) $R^1R^2 = NCH(Ph)Me$

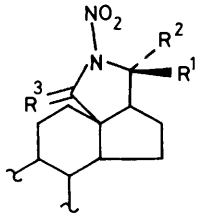
(36) $R^1 = NHCH(Ph)Me$, $R^2 = H$

(37) $R^1 = NH_2$, $R^2 = H$



(38) $R^1 = H$, $R^2 = NHNO_2$

(39) $R^1 = NHNO_2$, $R^2 = H$



(40) $R^1 = H$, $R^2 = Me$, $R^3 = H_2$

(41) $R^1 = Me$, $R^2 = H$, $R^3 = H, \sim OH$

(42) $R^1 = Me$, $R^2 = H$, $R^3 = O$

(43) $R^1 = Me$, $R^2 = H$, $R^3 = \alpha\text{-OAc}, \beta\text{-H}$

(44) $R^1 = Me$, $R^2 = H$, $R^3 = \alpha\text{-H}, \beta\text{-OAc}$

(45) $R^1 = Me$, $R^2 = H$, $R^3 = H_2$

imino compound (**8**). The reaction conditions and yields obtained with various oxidative systems are summarized in the Table (entries 1—6); best yields are observed with (diacetoxyiodo)benzene (DIB) (entry 4). No reaction was detected when this reagent was used in the presence of a catalytic amount of iodine (entry 5).

The structure of compound (**8**) was elucidated on the basis of spectral evidence. Its ^1H n.m.r. spectrum has no signal corresponding to a methyl group at C-10 whilst it showed an AB system at δ 3.62 and 3.77 (*J* 13 Hz) for the two protons at C-19. The ^{13}C n.m.r. spectrum displays the C-19 signal at δ 51.59 (DEPT experiment), and its molecular composition is in agreement with an accurate mass spectrometric measurement.

The cyclization of the related 6β-nitroaminocholestan-3β-yl acetate (**5**) proceeded analogously to give the epimine (**9**) (entries 7,8).

The double hydrogen-abstraction from the methyl group at C-10 observed during the intramolecular functionalization caused by alkoxy radicals at C-2 and C-4 has been explained on the basis of the hindered rotation of the 10-CH_2I group initially formed.[1,12] Similar behaviour was also observed during the photolysis of 2β-nitroaminocholestane (**13**) (entries 9,10) and 4β-nitroaminocholestane (**17**) (entry 11), where a double hydrogen-abstraction took place and the 19-acetyl derivatives (**20**) and (**21**) were formed. The examination of ^1H n.m.r. data of compounds (**20**) and (**21**) revealed that they were a mixture of 19*R* and 19*S* isomers (75:25) and (90:10) respectively. The more abundant 19*R* isomer could be separated from these mixtures by crystallization. The mechanism of this double functionalization is expected to be similar to that described for the alkoxy radicals and will not be commented upon here.[2]

In the pregnane series the intramolecular functionalization of the methyl group at C-13 was achieved from the 20*R*-nitroamine (**26**) (entries 12, 13). The best yield of the iodo compound (**27**) was obtained by photolysis of (**26**) in the presence of DIB. The structure of compound (**27**) was confirmed by means of ^1H and ^{13}C n.m.r. data. In particular, an AB system was observed at δ 3.26 and 3.05 for the two protons at C-18 and also the chemical shift for this carbon at δ 7.13. Cyclization of compound (**27**) to the nitroimino compound (**28**) was performed with silver acetate in acetone; in its ^1H n.m.r. spectrum the C-18 AB quartet has changed to a broad singlet at δ 3.70 ($w_{\frac{1}{2}}$ 4 Hz) and in the ^{13}C

n.m.r. spectrum the chemical shift for C-18 appears at δ 53.7 (DEPT experiment).

A similar situation was observed during the functionalization of the related pregnane nitroamine (**31**) (entry 14). The obtained iodo compound (**38**) was afterwards transformed into the cyclic compound (**40**).

However, a more complex reaction was noted when the isomeric 20*S*-nitroamine (**34**) was irradiated using HgO as oxidant (entry 15), the expected iodo nitroamine (**39**) and the doubly functionalized alcohol (**41**) being obtained. Further cyclization of compound (**39**) with silver acetate gave the 20*S*-nitroimino compound (**45**).

The structure of compound (**41**) is supported by the n.m.r. spectral data; *i.e.*, the downfield shift of the proton at C-18 (singlet at δ 5.51) and the chemical shift for this carbon at δ 92.21. When the photolysis of compound (**34**) was realized with DIB (entry 16), besides the alcohol (**41**) two new compounds were formed; the nitrolactam (**42**) and a mixture of C-18 acetyl derivatives (**43**) and (**44**). The nitrolactam (**42**) shows absorptions in its i.r. spectrum at 1 740 (CO) and 1 550 cm^{-1} (NO_2) and in its ^{13}C n.m.r. spectrum the signal for C-18 appears at δ 171.91. This compound (**42**) was also formed by pyridinium chlorochromate (PCC) oxidation of alcohol (**41**). Assignment of C-18 stereochemistry of acetyl derivatives (**43**) and (**44**) was made by a difference n.O.e. experiment. Irradiation of the C-20 methyl group resulted in a clean increase (11% after correction) of integration of the C-18 proton signal at δ 6.59 for the 18*S*-isomer (**43**).

The different behaviour of the C-20 nitroamine isomers can be explained if we consider the hindered rotation for C(13)–C(18) and C(17)–C(20) bonds in the initially formed 18-iodo derivatives (Figure). In the case of the (20*R*)-18-iodo-20-nitroamine a conformation as shown would hamper a second hydrogen abstraction, while the conformation displayed for the 20*S*-isomer agrees with the observed second hydrogen abstraction. Indeed, it is worthwhile to note that force field calculations carried out on side-chain conformers of both 5α-pregnane-3β,20-diols[13] indicate that rotamers analogous to those proposed in the Figure are the energetically favoured ones.

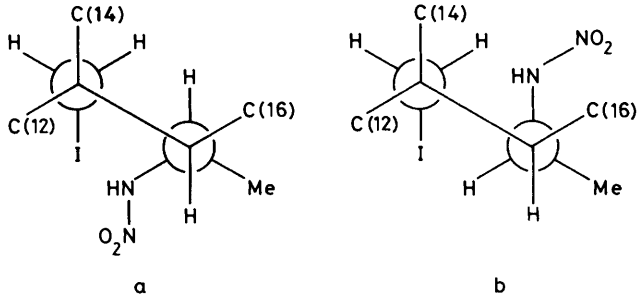
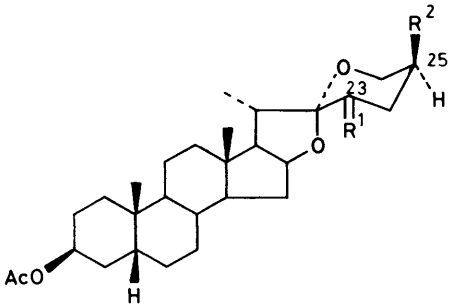


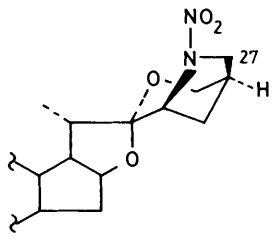
Figure. a, Conformation of the (20*R*) 18-iodonitroamine (**38**); b, Conformation of the (20*S*)-18-iodonitroamine (**39**)

Photolysis of the nitroamine (**46**) (entry 17) gave rise to the functionalization of the C-25 methyl group in the spirostan skeleton. Two compounds were obtained, the singly functionalized nitroimine (**48**) and an acid which was methylated with diazomethane to give its methyl ester (**47**). Both compounds

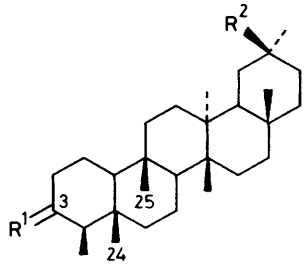


(**46**) R^1 = α-H, β-$NHNO_2$, R^2 = Me

(**47**) R^1 = α-H, β-N=N(O)OMe, R^2 = CO_2Me



(**48**)



(**49**) R^1 = NOH, R^2 = Me

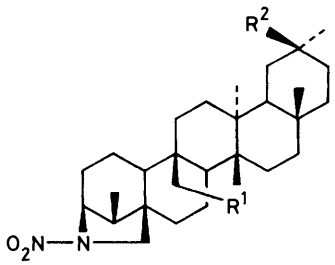
(**50**) R^1 = NOH, R^2 = CO_2Me

(**51**) R^1 = NNO_2, R^2 = Me

(**52**) R^1 = NNO_2, R^2 = CO_2Me

(**53**) R^1 = α-H, β-$NHNO_2$, R^2 = Me

(**54**) R^1 = α-H, β-$NHNO_2$, R^2 = CO_2Me



(**55**) R^1 = H, R^2 = Me

(**56**) R^1 = I, R^2 = Me

(**57**) R^1 = H, R^2 = CO_2Me

(**58**) R^1 = I, R^2 = CO_2Me

were identified on the basis of their high-resolution mass spectra and other spectral evidence. For example the i.r. spectrum of compound (**47**) shows absorption by the methyl *aci*-nitroamine function[14] at 1 550 cm^{-1} and in its ^1H n.m.r. spectrum the methoxy groups appear at δ 3.68 (CO_2Me) and 3.94 [N=NO(OMe)], since *O*-methylation of the nitroamine group also took place. Although the reaction of diazomethane with alkyl nitroamines may give *N*- or *O*-methyl derivatives[15] only the *O*-methylated product could be isolated in this case.

When the photolysis was performed with the nitroamino-friedelane derivatives (**53**) and (**54**) (entries 18, 19) two types of compounds were formed in each case, the expected *N*-nitroimines (**55**) and (**57**) and the iodo compounds (**56**) and (**58**). The structure of compounds (**56**) and (**58**) was confirmed by examination of the ^1H n.m.r. spectra. For example, two AB systems corresponding to protons at C-24 and C-25 can be observed, and the carbon bearing the iodine atom appears at δ 11.56 in the ^{13}C n.m.r. spectrum of compound (**56**).

This 'billiard' reaction has been previously observed in triterpenoid and diterpenoid skeletons, and is caused by the intramolecular hydrogen-abstraction of suitably placed alkoxyl radicals,[16] and cyanamide radicals.[4d]

In a preliminary communication we have demonstrated that DIB is a more efficient oxidant than the heavy-metal derivatives currently used in this type of reaction, in order to produce cyclic ethers from hydroxy compounds[17] and cyanoimine compounds from cyanamides.[4d] Such is indeed the case in most of the nitroamines shown in the Table (compare entries 1,2, and 3 with 4; 9 with 10; or 12 with 13). Furthermore, work-up is also easier with DIB and the amounts of the reagent and iodine needed are usually smaller; 1.5 mmol of DIB and 0.5 mmol of iodine per mmol of substrate are enough to drive the reaction to completion.

Experimental

M.p.s. were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured at room temperature for solutions in chloroform on a Perkin-Elmer 141 polarimeter. I.r. spectra were taken on a Perkin-Elmer 257 instrument in $CHCl_3$ solutions. ^1H N.m.r. spectra were recorded with a Perkin-Elmer R-12B (60 MHz), R-32 (90 MHz), or a Bruker WP200sy (200 MHz) instrument and ^{13}C n.m.r. spectra on a Bruker AC80 (20.1 MHz) or WP200sy (50.3 MHz) spectrometer 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 at 70 eV. T.l.c. was performed 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 vanillin (1 g) in H_2SO_4–EtOH (4:1; 200 ml). Circular layers of 1mm of Merck silica gel 60 PF254 were used on a Harrison Research Chromatotron for centrifugally assisted chromatography.

5α-*Cholestan*-6-*one* (**1**).—To a solution of cholest-5-ene (5.3 g) in a mixture of dry diethyl ether (150 ml) and boron trifluoride–diethylether (7 ml), under argon and at room temperature, was added slowly a suspension of lithium aluminium hydride (1.59 g) in diethyl ether (80 ml); after 1.5 h the excess of reagent was quenched with saturated aqueous Na_2SO_4, the solution was filtered, and the filtrate was evaporated under reduced pressure. To a solution of the residue (5 g), containing the borane, in tetrahydrofuran (THF) was added slowly at room temperature a solution of CrO_3 (3.1 g) in acetic acid (96%) (20 ml). After 24 h the reaction mixture was poured into water, neutralized, and extracted with chloroform. The extract was washed successively with aqueous hydrochloric acid (10%) and aqueous sodium hydrogen carbonate and concentrated under reduced pressure. Chromatography of the extract (hexane–ethyl acetate, 94:6) gave the title compound (**1**) (3.44 g); m.p. 99—101 °C (from methanol) (lit.,[18] 98—100 °C); $\nu_{max.}$(CCl_4) 1 710 cm^{-1} (CO); δ_H (90 MHz) 0.65 (3 H, s, 13-Me), 0.70 (3 H, s, 10-Me), and 0.86 (6 H, d, *J* 6 Hz, 25-Me_2).

6β-*Nitroamino*-5α-*cholestane* (**4**).—To a solution of the oxime (**2**) [m.p. 193—195 °C (from methanol) (lit.,[18] 204—206 °C)] (0.82 g) in dichloromethane (83 ml) and sodium nitrite (0.9 g) was added dropwise a mixture of glacial acetic acid (1.4 ml) and dichloromethane (73 ml) during 2 h and the mixture was then stirred for 3 h at room temperature and extracted with chloroform. The residue (0.93 g), containing 6-nitroimino-5α-cholestane (**3**), was dissolved in dry ethanol (70 ml) and to this solution was added slowly an excess of sodium borohydride (0.83 g) and the reaction mixture was stirred at room temperature for 2 h, then poured into water, extracted with chloroform, and the extract was concentrated. The residue (0.86 g) was purified by column chromatography (hexane–ethyl acetate, 96:4) to yield *nitroamine* (**4**) (0.58 g), amorphous, $[\alpha]_D$ −14.4° (*c* 0.32); $\nu_{max.}$ 3 410 (NH) and 1 570 cm^{-1} (NNO_2); $\lambda_{max.}$(EtOH) 239 nm (ε 5 330); δ_H (90 MHz) 0.66 (3 H, s, 13-Me), 0.85 (6 H, d, *J* 6 Hz, 25-Me_2), 0.95 (3 H, s, 10-Me), 4.25 (1 H, m, $w_{\frac{1}{2}}$ 9 Hz, 6-H), and 8.50 (1 H, m, $w_{\frac{1}{2}}$ 9 Hz, $NHNO_2$); *m/z* 386.3741 ($M^+ - NO_2$, 30% $C_{27}H_{48}N$ requires *m/z*, 386.3744), 370 ($M - NH_2NO_2$, 59), and 369 (21).

N-*Nitro*-6β,19-*epimino*-5α-*cholestane* (**8**).—(a) *With lead tetra-acetate–iodine*. A mixture of nitroamine (**4**) (0.35 g, 0.81 mmol), iodine (0.3 g, 1.18 mmol), and lead tetra-acetate (LTA) (0.88 g, 2 mmol) in cyclohexane was irradiated with two 150 W tungsten-filament lamps, while being refluxed, for 2 h. Then the reaction mixture was poured into water and extracted with chloroform, and the extract was washed several times with aqueous sodium thiosulphate. After concentration the residue was purified by column chromatography (hexane–ethyl acetate, 99:1) to yield the *imino compound* (**8**) (0.18 g, 51%), m.p. 117—118 °C (from methanol); $[\alpha]_D$ −55.5° (*c* 0.38); $\nu_{max.}$ 1 570 cm^{-1} (NNO_2); $\lambda_{max.}$ 244 nm (6 020); δ_H(200 MHz) 0.66 (3 H, s, 13-Me), 0.85 (6 H, d, *J* 6 Hz, 25-Me_2), 3.62 and 3.77 (2 H, AB_q, *J* 13 Hz, 19-H_2), and 4.33 (1 H, d, *J* 4.3 Hz, 6-H); δ_C(50.3 MHz) 12.55 (C-18), 18.72 (C-21), 21.86 (C-2), 22.00 (C-11), 22.68 (C-27), 22.94 (C-26), 23.60 (C-23), 23.97 (C-15), 24.33 (C-3), 26.86 (C-7), 28.14 (C-25), 28.31 (C-16), 29.03 (C-4), 32.95 (C-1), 35.25 (C-8), 35.83 (C-20), 36.26 (C-22), 39.61 (C-24), 39.89 (C-12), 43.2 (C-10), 43.25 (C-13), 50.49 (C-5), 51.59 (C-19), 55.00 (C-9), 55.21 (C-14), 56.28 (C-17), and 65.63 (C-6); *m/z* 431.3607 (M^+ + H, 0.1%. $C_{27}H_{47}N_2O_2$ requires *m/z*, 431.3577), 413.3556 (7.5. $C_{27}H_{45}N_2O$ requires *m/z*, 413.3532, and 384.3595 ($M - NO_2$, 100. $C_{27}H_{46}N$ requires *m/z*, 384.3630).

(b) *With mercury*(II) *acetate–iodine*. A mixture of nitroamine (**4**) (0.15 g, 0.35 mmol), iodine (0.13 g, 0.5 mmol), and $Hg(OAc)_2$ (0.27 g, 0.85 mmol) in cyclohexane (35 ml) was irradiated and stirred for 3 h at 40—50 °C. After usual work-up and purification of the crude product, imine-compound (**8**) was obtained in 73% yield.

(c) *With mercury*(II) *oxide–iodine*. A mixture of nitroamine (**4**) (29 mg, 0.06 mmol), iodine (33 mg, 0.13 mmol), and yellow HgO (53 mg, 0.24 mmol) in cyclohexane (12 ml) was refluxed while being irradiated for 5 h. After usual work-up and purification compound (**8**) was obtained in 69% yield.

(d) *With* (*diacetoxyiodo*)*benzene–iodine*. A mixture of nitroamine (**4**) (95 mg, 0.22 mmol), iodine (29 mg, 0.11 mmol), and DIB (111 mg, 0.34 mmol) in cyclohexane (25 ml) was irradiated under reflux for 70 min. After usual work-up and purification the imine compound (**8**) (73 mg, 77%) was obtained. When the reaction was performed under the same conditions

but using 0.1 equiv. of I_2 instead of 0.5 equiv. no reaction was observed.

(e) *With iodosylbenzene–iodine.* A mixture of nitroamine (**4**) (46 mg, 0.1 mmol), iodine (13 mg, 0.05 mmol), and iodosylbenzene (32 mg, 0.14 mmol) in cyclohexane (20 ml) was irradiated under reflux for 5 h. The starting material was recovered and only traces of imine compound (**8**) were detected.

N-*Nitro*-6β,19-*epimino*-5α-*cholestan*-3β-*yl Acetate* (**9**).—*Method A.* A mixture of nitroamine (**5**) (400 mg, 0.82 mmol), iodine (150 mg, 0.59 mmol), and LTA (1.8 g, 4.06 mmol) in cyclohexane (60 ml) was irradiated, under reflux, under the above mentioned conditions, for 2 h. The reaction mixture was then poured into water and worked up as usual; the crude product was purified by column chromatography (benzene–ethyl acetate, 99:1) to give *imine compound* (**9**) (250 mg, 63%), amorphous; $\lambda_{max.}$ 241 nm (7 400); $\nu_{max.}$ 1 730 (CO) and 1 490 cm^{-1}; δ_H (90 MHz) 0.66 (3 H, s, 13-Me), 0.81 (6 H, d, *J* 6 Hz, 25-Me_2), 2.0 (3 H, s, MeCO), 3.73 (2 H, br s, $w_{\frac{1}{2}}$ 4 Hz, 19-H_2), 4.39 (1 H, d, *J* 4 Hz, 6-H), and 4.60 (1 H, m, $w_{\frac{1}{2}}$ 16 Hz, 3-H); δ_C (20.1 MHz) 12.4 (C-18), 18.6 (C-21), 21.2 (CH_3CO), 22.2 (C-11), 22.55 (C-26), 22.8 (C-27), 23.5 (C-23), 23.8 (C-15), 27.2 (C-7), 27.7 (C-2), 28.0 (C-25), 28.2 (C-16), 31.9 (C-4), 32.8 (C-1), 35.05 (C-8), 35.7 (C-20), 36.1 (C-22), 39.5 (C-24), 39.7 (C-12), 42.4 (C-13), 43.2 (C-10), 49.4 (C-5), 51.2 (C-19), 54.3 (C-9), 55.1 (C-14), 56.1 (C-17), 65.1 (C-6), 71.0 (C-3), and 170.4 (CH_3CO); *m/z* 505 (c.i. $M^+ + NH_3$), 488 (*M*, 0.1%), 442.3767 ($M - NO_2$, 57. $C_{29}H_{48}NO_2$ requires *m/z*, 442.3685), and 383.3560 (4. $C_{27}H_{45}N$ requires *m/z*, 383.3552).

Method B. A mixture of nitroamine (**5**) (200 mg, 0.41 mmol), iodine (1 g, 3.9 mmol), and yellow HgO (2 g, 9.2 mmol) in cyclohexane (30 ml) was irradiated under reflux under the aforementioned conditions for 2 h. The reaction mixture was then filtered, and the filtrate was poured into water and worked-up as usual. After purification by column chromatography, compound (**9**) (120 mg, 60%) was obtained.

5α-*Cholestan*-2-*one* (**10**) *and* 5α-*Cholestan*-4-*one* (**14**).—To a solution of the tosylhydrazone (**7**), m.p. 162—163 °C (from methanol) (lit.,[19] 168—170 °C); δ_H(90 MHz) 0.65 (3 H, s, 13-Me), 0.80 (3 H, s, 10-Me), 0.85 (6 H, s, *J* 6 Hz, 25-Me_2), and 7.30 and 7.85 (4 H, m, OTs) (2.32 g) in a mixture of dry THF (10 ml) and tetramethylethylenediamine (12 ml), under argon and cooled to −50 °C, was added butyl-lithium (1.6M solution in hexane; 6.69 ml, 10.7 mmol). When the reaction mixture became red, $(MeS)_2$ (0.5 ml) was added; the solution turned yellow and it was allowed to warm to room temperature and was stirred until nitrogen evolution ceased and then was cooled again to −50 °C with addition of another portion (6 ml) of the 1.6M-solution of BuLi in hexane, the mixture becoming red once more. The reaction mixture was allowed to warm to room temperature, then was poured into water and extracted with dichloromethane in the usual way to yield a mixture of methyl vinyl sulphides (**18**) and (**19**) in the ratio 2.5:1 as indicated by ^1H n.m.r. spectroscopy. Hydrolysis of the vinyl sulphides was performed as follows: to a solution of the mixture of (**18**) and (**19**) (12 g) in dioxane (200 ml) was added a mixture of dioxane–water (4:1) (250 ml) and $HgCl_2$ (24 g). The reaction mixture was stirred for 4 days at 80 °C, and then filtered through Celite, the filter was washed with diethyl ether, and the organic layer was concentrated under reduced pressure. The crude product was purified by column chromatography (hexane–benzene, 55:45) to yield starting material (1.7 g) and a mixture (2.3 g) that was resolved by chromatography in a Chromatotron (hexane–ethyl acetate, 97:3) to yield ketones (**10**) (1.42 g) and (**14**) (0.6 g), m.p. 128—129 °C (from methanol) (lit.,[20] 130 °C) and m.p. 96—98 °C (from methanol) (lit.,[18] 98—100 °C), respectively. Hydrolysis of the mixture of sulphides was also attempted by the following methods: $HgCl_2$ in acetonitrile–water, 3:1 at reflux for 20 h; with hydrochloric acid–dioxane, 1:4 at 60 °C for 40 h; with trifluoroacetic acid–chloroform, 1:4, 1:1, and 7:3 at room temperature for 60 h; but no success was achieved in these cases.

2β-*Nitroamino*-5α-*cholestane* (**13**).—To a solution of the oxime (**11**) {m.p. 200—202 °C (from methanol); $[\alpha]_D$ +13.7° (*c* 1.0) (lit.,[20] 200 °C)} (1.1 g) in dichloromethane (60 ml) were added sodium nitrite (1.2 g) and then dropwise a mixture of glacial acetic acid (2.5 ml) and dichloromethane (13 ml) for 1 h. The reaction mixture was kept at room temperature and stirred for 2.5 h and was then poured into water and extracted with dichloromethane in the usual way. The crude extract residue containing the nitroimine (**12**) was dissolved in dry ethanol (500 ml), and to this stirred solution an excess of sodium borohydride (1 g) was added slowly during 2 h. Then the mixture was poured into water and worked-up as usual. After purification of the residue by column chromatography (hexane–ethyl acetate, 96:4) the *nitroamine* (**13**) (350 mg) was obtained, m.p. 153—155 °C (from methanol); $[\alpha]_D$ +23.1° (*c* 0.32); $\nu_{max.}$ 3 410 (NH) and 1 570 cm^{-1} (NNO_2); $\lambda_{max.}$ (ethanol) 239 nm (5 040); δ_H(90 MHz) 0.65 (3 H, s, 13-Me), 0.90 (3 H, s, 10-Me), 4.20 (1 H, m, $w_{\frac{1}{2}}$ 18 Hz, 2-H), and 8.45 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, $NHNO_2$); *m/z* 432.3688 (M^+, 1.3%. $C_{27}H_{48}N_2O_2$ requires *M*, 432.3717), 386 ($M - NO_2$, 7), and 370 ($M - NH_2 - NO_2$, 19).

N-*Nitro*-2β,19-*epimino*-5α-*cholestan*-19-*yl Acetate* (**20**).—*Method A.* A mixture of the nitroamine (**13**) (50 mg, 0.11 mmol), iodine (43 mg, 0.17 mmol), and LTA (125 mg, 0.28 mmol) in cyclohexane (30 ml) was irradiated under reflux, as described before, for 2 h. The reaction mixture was then poured into water and extracted with dichloromethane. The extracts were washed with aqueous sodium thiosulphate, and after concentration the extract was purified by Chromatotron (hexane–ethyl acetate, 97:3) to give the title compound (28 mg, 50%), as a mixture of 19*R* and 19*S* isomers (75:25 by ^1H n.m.r.) from which the 19*R isomer* (**20**) was purified by crystallization, m.p. 140—142 °C (from methanol); $[\alpha]_D$ +43.5° (*c* 0.2); $\nu_{max.}$ 1 750 (CO) and 1 515 cm^{-1} (NNO_2); δ_H (200 MHz) 0.56 (3 H, s, 13-Me), 0.83 (6 H, d, *J* 6.4 Hz, 25-Me_2), 2.13 (3 H, s, MeCO), 4.27 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, 2-H), and 6.63 (1 H, s, 19-H); *m/z* 441.3601 ($M^+ - NO_2H$, 3%. $C_{29}H_{47}NO_2$ requires *m/z*, 441.3607), 382 (M – AcOH – NO_2, 15), 371 (12.5), and 355 (25).

Method B. A mixture of nitroamine (**13**) (45 mg, 0.1 mmol), iodine (30 mg, 0.12 mmol), and DIB (80 mg, 0.25 mmol) in cyclohexane (20 ml) was irradiated under reflux as described above for 1.5 h. The reaction mixture was then worked up as usual, and the extract, after concentration, was purified by chromatotron (hexane–ethyl acetate, 97:3) to give the imino compound (**20**) (33 mg, 64%).

4β-*Nitroamino*-5α-*cholestane* (**17**).—To a mixture of the oxime (**15**) {m.p. 216—217 °C (from $CHCl_3$); $[\alpha]_D$ +101° (*c* 0.28) (lit.,[18] 219—222 °C; $[\alpha]_D$ +114.5°); $\nu_{max.}$ 3 260 cm^{-1}; δ_H(200 MHz) 0.64 (3 H, s, 13-Me), 0.76 (3 H, s, 10-Me), 0.86 (6 H, d, *J* 6.4 Hz, 25-Me_2), 0.89 (3 H, d, *J* 6.9 Hz, 20-Me), and 9.0 (1 H, m, $w_{\frac{1}{2}}$ 8 Hz, NOH); *m/z* 401 (M^+, 66%), 384 (M – OH, 100), 369 (21), and 246 (79)} (500 mg), dichloromethane (32 ml), and sodium nitrite (650 mg) was added dropwise a solution of glacial acetic acid (1.2 ml) in dichloromethane (5.1 ml). The mixture was kept at room temperature and stirred for 2.5 h and then worked up as usual. The crude product containing the nitroimine (**16**) (500 mg) was dissolved in dry ethanol (200 ml), and to this solution an excess of sodium borohydride (400 mg) was added slowly during 2 h. Then the reaction mixture was poured into water and extracted with dichloromethane. After purification of the residue by Chromatotron (hexane–ethyl

acetate, 96:4) the *title compound* (**17**) (330 mg) was obtained, m.p. 162—164 °C (from methanol); $[\alpha]_D$ +56.5° (*c* 0.26); $\nu_{max.}$ 3 340 (NH) and 1 570 cm^{-1}; δ_H(200 MHz) 0.63 (3 H, s, 13-Me), 0.91 (3 H, s, 10-Me), 0.86 (6 H, d, *J* 6.6 Hz, 25-Me_2), 4.20 (1 H, m, $w_{\frac{1}{2}}$ 12.5 Hz, 4-H), and 8.46 (1 H, m, $w_{\frac{1}{2}}$ 12.5 Hz, $NHNO_2$); *m/z* 432.3695 (M^+, 18%. $C_{27}H_{48}N_2O_2$ requires *M*, 432.3717), 402.3612 (11. $C_{26}H_{46}N_2O$ requires *m/z*, 402.3610), 386.3745 (*M* − NO_2, 72. $C_{27}H_{48}O$ requires *m/z* 386.3745), 370.3615 (*M* − NH_2NO_2, 100. $C_{27}H_{46}$ requires *m/z*, 370.3600), and 355.3356 (43. $C_{26}H_{43}$ requires *m/z*, 355.3365).

N-*Nitro*-4β, 19-*epimino*-5α-*cholestan*-19-*yl Acetate* (**21**).—A mixture of the nitroamine (**17**) (225 mg, 0.52 mmol), iodine (191 mg, 0.75 mmol), and LTA (562 mg, 1.27 mmol) in cyclohexane (40 ml) was irradiated under reflux for 2 h, as described above. Then the reaction mixture was worked up as usual and the crude product was purified by Chromatotron (hexane–ethyl acetate, 97:3) to yield starting material (23 mg), and the title compound (**21**) (118 mg, 53%) as a mixture of 19*R* and 19*S* isomers (90:10 by ^1H n.m.r.) from which the 19*R isomer* (**21**) was purified by crystallization, m.p. 148—151 °C (from methanol); $[\alpha]_D$ +51° (*c* 0.18); $\nu_{max.}$ 1 750 (CO) and 1 510 cm^{-1} (NNO_2); δ_H(200 MHz) 0.59 (3 H, s, 13-Me), 0.85 (6 H, d, *J* 6.5 Hz, 25-Me_2), 0.86 (3 H, d, *J* 6.4 Hz, 20-Me), 2.15 (3 H, s, $MeCO_2$), 4.29 (1 H, d, *J* 4.0 Hz, 4-H), and 6.66 (1 H, s, 19-H); *m/z* 441.3605 (M^+ − NO_2H, 11%. $C_{29}H_{47}NO_2$ requires *m/z*, 441.3607), 400.3555 (14. $C_{27}H_{46}NO$ requires *m/z*, 400.3580), 382.3531 (*M* − AcOH − NO_2, 100. $C_{27}H_{44}N$ requires *m/z*, 382.3473), 355.3359 (59. $C_{26}H_{43}$ requires *m/z*, 355.3364).

Cyclization of (20R)-20-*Nitroaminopreg*-5-*en*-3β-*yl Acetate* (**26**).—*Method A*. A mixture of nitroamine (**26**) (2 g, 4.95 mmol) in dichloromethane (250 ml), iodine (4 g, 15.7 mmol), and yellow HgO (4 g, 18.4 mmol) was irradiated at 40—50 °C with two 150 W tungsten-filament lamps for 1.5 h. Then the reaction mixture was filtered and the filtrate was poured into a saturated aqueous sodium thiosulphate, and extracted with dichloromethane. After column chromatography (hexane–ethyl acetate, 88:12) (20*R*)-18-iodo-20-nitroaminopregn-5-en-3β-yl acetate (**27**) (660 mg, 25%) was obtained, m.p. 192—194 °C (from hexane–ethyl acetate); $\nu_{max.}$ 3 390 (NH), 1 730 (CO), and 1 575 cm^{-1} (NNO_2); $\lambda_{max.}$ 224 nm (10 300); δ_H (90 MHz) 1.0 (3 H, s, 10-Me), 1.15 (3 H, d, *J* 7 Hz, 20-Me), 2.0 (3 H, s, $MeCO_2$), 3.26, 3.05 (2 H, AB_q, *J* 11 Hz, 18-H_2), 4.25 (1 H, m, $W_{\frac{1}{2}}$ 24 Hz, 20-H), 4.6 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 3-H), 5.37 (1 H, m, $w_{\frac{1}{2}}$ 9 Hz, 6-H), and 9.1 (1 H, m, $w_{\frac{1}{2}}$ 15 Hz, NH); δ_C(20.1 MHz) 7.13 (C-18), 18.1 (C-21), 19.2 (C-19), 20.5 (C-11), 21.4 (CH_3CO), 23.9 (C-15), 26.2 (C-16), 27.6 (C-2), 31.55 (C-7), 32.3 (C-8), 36.6 (C-10), 36.95 (C-1), 38.0 (C-4), 39.4 (C-12), 43.6 (C-13), 49.6 (C-9), 52.5 (C-17), 53.75 (C-20), 55.9 (C-14), 73.9 (C-3), 121.8 (C-6), 139.9 (C-5), and 171.0 (CH_3CO); *m/z* (15 eV) 470 (M^+ − NO_2, 66%), 408 (32), and 342 (100).

Method B. A mixture of nitroamine (**26**) (68 mg, 0.17 mmol), iodine (21 mg, 0.08 mmol), and DIB (80 mg, 0.25 mmol) in dry dichloromethane (40 ml) was irradiated for 1.5 h as described in method A. After usual work-up and purification of the crude product, iodo compound (**27**) was obtained in 47% yield.

(20R)-N-*Nitro*-18,20-*epiminopregn*-5-*en*-3β-*yl Acetate* (**28**).—To a solution of iodonitroamine (**27**) (90 mg) in acetone (20 ml) was added silver acetate (150 mg) and the reaction mixture was stirred in darkness for 18 h. Then the mixture was filtered, the filtrate concentrated under reduced pressure, and the residue purified by column chromatography (benzene–ethyl acetate, 98:2) to give the imino compound (**28**) (50 mg, 71%), m.p. 190—192 °C (acetone–hexane); $\nu_{max.}$ 1 725 and 1 490 cm^{-1} (NNO_2); $\lambda_{max.}$ 243 nm (9 100); δ_H(90 MHz) 0.98 (3 H, s, 10-Me), 1.38 (3 H, d, *J* 6 Hz, 20-Me), 2.03 (3 H, s, $MeCO_2$), 3.70 (2 H, br s, $w_{\frac{1}{2}}$ 4 Hz, 18-H_2), 4.38 (1 H, m, *J* 6 Hz, 20-H), 4.6 (1 H, m, $w_{\frac{1}{2}}$ 26 Hz, 3-H), and 5.37 (1 H, m, $w_{\frac{1}{2}}$ 9 Hz, 6-H); δ_C(20.1 MHz) 18.8 (C-21), 19.4 (C-19), 21.4 (CH_3CO), 22.6 (C-11), 25.6 (C-15), 27.7 (C-2), 31.4 (C-16), 31.7 (C-7), 33.9 (C-8), 36.5 (C-10), 37.0 (C-1 and C-12), 38.1 (C-4), 49.25 (C-9), 51.8 (C-13), 53.5 (C-17), 53.7 (C-18), 55.45 (C-14), 65.5 (C-20), 73.7 (C-3), 121.9 (C-6), 139.6 (C-5), and 171.0 (CH_3CO); *m/z* 356 (15 eV) (M^+ − NO_2, 0.4%), 342 (*M* − AcOH, 27), 325 (13), 296 (10), 295 (13), 105 (69), and 91 (100).

(20R)-20-*Aminopregn*-5-*en*-3β-*ol* (**22**) *and* (20S)-20-*Aminopregn*-5-*en*-3β-*ol* (**24**).—To a stirred solution of 3β-hydroxypregn-5-en-20-one oxime (5.5 g), prepared from the easily available corresponding ketone, in dry propan-1-ol (350 ml) was added sodium (13 g) in small portions during 2 h and then saturated aqueous NaCl (100 ml) was added and the mixture was stirred for 10 min. After work-up the organic extract was purified by column chromatography on Al_2O_3 grade II (270 g) (dichloromethane–ethanol, 996:4) to yield the 20*R* amine (**22**) (2.9 g), 20*S* amine (**24**) (2.21 g), and a mixture of both (0.3 g). The 20*R* amine (**22**) had m.p. 216—218 °C (lit.,[8] 217 °C); δ_H(90 MHz) 0.75 (3 H, s, 13-Me), 1.0 (3 H, s, 10-Me), 3.5 (1 H, m, $w_{\frac{1}{2}}$ 26 Hz, 3-H), and 5.3 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, 6-H). The 20*S* amine (**24**) had m.p. 177—179 °C from ethyl acetate) (lit.,[8] 177 °C); δ_H(60 MHz) 0.67 (3 H, s, 13-Me), 1.0 (3 H, s, 10-Me), 1.13 (3 H, d, *J* 6 Hz, 20-Me), 3.5 (1 H, $w_{\frac{1}{2}}$ 20 Hz, 3-H), and 5.3 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, 6-H).

(20R)-20-*Ethoxycarbonylaminopregn*-5-*en*-3β-*yl Acetate* (**23**).—To a solution of the 20*R* amine (**22**) (2.9 g) in dichloromethane (100 ml), cooled to −5 °C, was added ethyl chloroformate (0.62 ml) dropwise. This solution was kept at −5 °C for 25 min and then NaOH (0.1M; 21 ml) was added and the mixture was stirred for 30 min, then diluted with dichloromethane, and the organic layer was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The crude residue (2.9 g) was dissolved in pyridine (50 ml), and acetic anhydride (13 ml) was added. The mixture was stirred for 3 h at room temperature and then worked up as usual. The residue was purified by column chromatography (hexane–ethyl acetate, 86:14) to yield carbamate (**23**) (2.1 g) δ_H(90 MHz) 0.72 (3 H, s, 13-Me), 1.00 (3 H, s, 10-Me), 1.05 (3 H, d, *J* 7 Hz, 20-Me), 1.2 (3 H, t, *J* 6 Hz, CO_2CH_2Me), 2.0 (3 H, s, $MeCO_2$), 3.6 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 20-H), 4.1 (2 H, q, *J* 6 Hz, CO_2CH_2Me), 4.5 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 3-H), and 5.35 (1 H, m, $w_{\frac{1}{2}}$ 11 Hz, 6-H).

(20S)-20-*Ethoxycarbonylaminopregn*-5-*en*-3β-*yl Acetate* (**25**).—The experimental procedure from amine (**24**) is the same as that described previously for the preparation of carbamate (**23**). The crude residue was purified by column chromatography (hexane–ethyl acetate, 86:14) to yield the pure carbamate (**25**) (2.08 g), δ_H(90 MHz) 0.70 (3 H, s, 13-Me), 1.0 (3 H, s, 10-Me), 1.15 (3 H, d, *J* 7 Hz, 20-Me), 2.0 (3 H, s, $MeCO_2$), 3.6 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 20-H), 4.1 (2 H, q, *J* 9 Hz, CO_2CH_2Me), 4.5 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 3-H), and 5.35 (1 H, m, $w_{\frac{1}{2}}$ 11 Hz, 6-H).

(20R)-20-*Ethoxycarbonylamino*-5α-*pregnan*-3β-*yl Acetate* (**29**).—To a solution of carbamate (**23**) (1.8 g) in glacial acetic acid (75 ml) was added PtO_2 (912 mg) and the stirred reaction mixture was kept overnight under H_2, then poured into water, neutralized with sodium hydrogen carbonate, and extracted with dichloromethane to give, after concentration, the title compound (**29**) (1.75 g), δ_H(90 MHz) 0.70 (3 H, s, 13-Me), 0.80 (3 H, s, 10-Me), 1.05 (3 H, d, *J* 7 Hz, 20-Me), 2.0 (3 H, s, $MeCO_2$), 3.60 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 20-H), 4.1 (2 H, q, *J* 9 Hz, CO_2CH_2Me), and 4.5 (1 H, m, $W_{\frac{1}{2}}$ 21 Hz, 3-H).

(20R)-20-*Ethoxycarbonyl*(*nitro*)*amino*-5α-*pregnan*-3β-*yl Acetate* (**30**).—A solution of carbamate (**29**) (1.7 g) in the

smallest volume of glacial acetic acid was cooled to −60 °C and then a mixture of conc. nitric acid–acetic anhydride (14.5:1) (22.4 ml) also cooled to −60 °C was added. The reaction mixture was allowed to warm to room temperature, kept overnight, and then poured into water, neutralized with aqueous sodium hydrogen carbonate, and extracted with dichloromethane. The extract was purified by column chromatography (hexane–ethyl acetate, 90:10) to give *nitrocarbamate* (**30**) (1.1 g), m.p. 144—146 °C (from methanol); $[\alpha]_D$ +30° (*c* 0.22); $\nu_{max.}$ 1 730 (CO) and 1 570 cm^{-1} (NNO_2); δ_H(90 MHz) 0.65 (3 H, s, 13-Me), 0.82 (3 H, s, 10-Me), 1.33 (3 H, d, *J* 7 Hz, 20-Me), 1.38 (3 H, t, *J* 7 Hz, CO_2CH_2Me), 2.2 (3 H, s, $MeCO_2$), 4.35 (2 H, q, *J* 7 Hz, CO_2CH_2Me), and 4.6 (2 H, m, $w_{\frac{1}{2}}$ 54 Hz, 3-H, 20-H); *m/z* 432.3115 ($M^+ - NO_2$, 1%. $C_{26}H_{42}NO_4$ requires *m/z*, 432.3112), 418 ($M - CH_3CO_2H$, 2.2), and 344 (4.6).

(20R)-20-*Nitroamino*-5α-*pregnan*-3β-*yl Acetate* (**31**).—A solution of carbamate (**30**) (1.52 g) in the smallest volume of ethanol was cooled to 0 °C and NH_4OH (3 ml) was added. The mixture was allowed to warm to room temperature, stirred for 18 h, and poured into water, and dil. HCl was then added (to pH 4), to be followed by the usual work-up. After chromatography of the residue by Chromatotron (benzene–ethyl acetate, 97:3), *nitroamine* (**31**) (562 mg) was obtained, m.p. 202—204 °C (from methanol); $[\alpha]_D$ +3.3° (*c* 0.24); $\nu_{max.}$ 3 390 (NH), 1 720 (CO), and 1 570 cm^{-1} (NNO_2); δ_H (90 MHz) 0.72 (3 H, s, 13-Me), 0.83 (3 H, s, 10-Me), 1.19 (3 H, d, *J* 6.6 Hz, 20-Me), 2.2 (3 H, s, $MeCO_2$), 4.15 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 20-H), 4.7 (1 H, m, $w_{\frac{1}{2}}$ 27 Hz, 3-H), and 8.75 (1 H, m, $w_{\frac{1}{2}}$ 24 Hz, $NHNO_2$); *m/z* 360.2888 ($M^+ - NO_2$, 2.5%. $C_{23}H_{38}NO_2$ requires *m/z*, 360.2902), 344.2714 ($M - NH_2NO_2$, 5.9. $C_{23}H_{36}O_2$ requires *m/z*, 344.2714), 329.2484 (2.3. $C_{22}H_{33}O_2$ requires *m/z*, 329.2480), and 269.2278 (4.1. $C_{20}H_{29}$ requires *m/z*, 269.2269).

(20R)-18-*Iodo*-20-*nitroamino*-5α-*pregnan*-3β-*yl Acetate* (**38**).—A mixture of amine (**31**) (450 mg, 1.1 mmol), iodine (900 mg, 3.54 mmol), and yellow HgO (900 mg, 4.15 mmol) in dry dichloromethane (45 ml) was irradiated, whilst stirred under nitrogen, at 45—50 °C with two 150 W tungsten-filament lamps for 1.5 h. The reaction mixture was then poured into water and extracted with dichloromethane. The extracts were washed with aqueous sodium thiosulphate. After concentration the crude product was purified by Chromatotron (hexane–ethyl acetate, 80:20) to give *iodo compound* (**38**) (164 mg), m.p. 176—178 °C (from acetone–hexane); $[\alpha]_D$ −8.4° (*c* 0.26); $\nu_{max.}$ 3 400 (NH), 1 720 (CO), and 1 570 cm^{-1} (NNO_2); δ_H(90 MHz) 0.83 (3 H, s, 10-Me), 1.26 (3 H, d, *J* 6 Hz, 20-Me), 2.03 (3 H, s, $MeCO_2$), 3.28 and 3.04 (2 H, AB_q, *J* 11 Hz, 18-H_2), 4.2 (1 H, m, $w_{\frac{1}{2}}$ 24 Hz, 20-H), 4.65 (1 H, m, $w_{\frac{1}{2}}$ 24 Hz, 3-H), and 8.95 (1 H, $w_{\frac{1}{2}}$ 12 Hz, $NHNO_2$); *m/z* 470.1717 ($M^+ - NH_2NO_2$, 33%. $C_{23}H_{35}IO_2$ requires *m/z*, 470.1683) and 389.2465 (29. $C_{22}H_{33}N_2O_4$ requires *m/z*, 389.2430).

(20R)-N-*Nitro*-18,20-*epimino*-5α-*pregnan*-3β-*yl Acetate* (**40**).—A mixture of iodo compound (**38**) (93 mg) and silver acetate (150 mg) in dry acetone (30 ml) was kept in darkness and stirred for 24 h, and then another portion of silver acetate (150 mg) was added to complete the reaction. After 24 h the mixture was poured into water and extracted with dichloromethane. After concentration the crude product was purified by Chromatotron (hexane–ethyl acetate, 91:9) to yield *imino compound* (**40**) (40 mg, 57%), m.p. 208—210 °C (from methanol); $[\alpha]_D$ +6° (*c* 0.2); $\nu_{max.}$ 1 720 (CO) and 1 490 cm^{-1} (NNO_2); δ_H (200 MHz) 0.75 (3 H, s, 10-Me), 1.35 (3 H, d, *J* 6.5 Hz, 20-Me), 1.99 (3 H, s, $MeCO_2$), 3.55 and 3.68 (2 H, ABq, *J* 12.7 Hz, 18-H_2), 4.20 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, 20-H), and 4.65 (1 H, m, $W_{\frac{1}{2}}$ 12.5 Hz, 3-H); *m/z* 389.2460 ($M^+ - CH_3$, 10%. $C_{22}H_{33}N_2O_4$ requires *m/z*, 389.2440), 358.2755 ($M - NO_2$, 78. $C_{23}H_{36}NO_2$ requires *m/z*, 358.2740), and 344.2505 ($M - CH_3CO_2H$, 41. $C_{21}H_{32}N_2O_2$ requires *m/z*, 344.2464).

(20S)-20-*Ethoxycarbonylamino*-5α-*pregnan*-3β-*yl Acetate* (**32**).—*Method A*. A mixture of carbamate (**25**) (1.9 g) in glacial acetic acid and PtO_2 (912 mg) was hydrogenated under the conditions described for the preparation of compound (**29**). After purification *carbamate* (**32**) was obtained (1.2 g), m.p. 169—171 °C (from acetone–hexane); $[\alpha]_D$ −3° (*c* 0.18); $\nu_{max.}$ 3 420 (NH) and 1 710 and 1 510 cm^{-1} (CO); δ_H(200 MHz) 0.70 (3 H, s, 13-Me), 0.82 (3 H, s, 10-Me), 1.15 (3 H, d, *J* 6.4 Hz, 20-Me), 1.23 (3 H, t, *J* 7.2 Hz, CO_2CH_2Me), 2.02 (3 H, s, $MeCO_2$), 3.64 (1 H, m, $w_{\frac{1}{2}}$ 30 Hz, 20-H), 4.10 (2 H, q, *J* 6.9 Hz, CO_2CH_2Me), 4.53 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, NH), and 4.68 (1 H, m, $w_{\frac{1}{2}}$ 25 Hz, 3-H); δ_C(20.1 MHz) 12.18 (C-18), 12.29 (C-19), 14.63 ($NHCO_2CH_2CH_3$), 21.03 (CH_3CO), 21.33 (C-11), 22.04 (C-21), 23.90 (C-15), 26.51 (C-12), 27.48 (C-2), 28.56 (C-6), 31.61 (C-1), 31.94 (C-7), 34.04 (C-4), 35.35 (C-8), 35.51 (C-10), 39.29 (C-16), 42.02 (C-13), 44.75 (C-5), 49.64 (C-9), 54.28 (C-17), 56.48 (C-14), 57.14 (C-20), 60.44 ($NHCO_2CH_2Me$), 73.67 (C-3), 155.91 ($NHCO_2$), and 170.53 (CO); *m/z* 344.2710 ($M^+ - NH_2CO_2Et$, 1.2%. $C_{23}H_{36}O_2$ requires *m/z*, 344.2714), 316.2343 (0.5. $C_{21}H_{32}O_2$ requires *m/z*, 316.2400), and 256.2218 (0.7. $C_{19}H_{28}$ requires *m/z*, 256.2189).

Method B. A solution of 20-oxo-5α-pregnan-3β-yl acetate (15 g), (*S*)-(−)-phenylethylamine (6.75 g), and PTSA (1.5 g) in toluene (150 ml) was refluxed under argon with a Dean–Stark apparatus to remove the generated water. The reaction, monitored by n.m.r. spectroscopy, was continued for 4 days and then the reaction mixture was concentrated to give the imine (**35**), which was used without further purification in the following reaction.

To a solution of imine (**35**) (15 g) in THF (260 ml) cooled to 0 °C was added a 1M solution of BH_3·THF (64 ml) and the mixture was kept at room temperature for 6 h, then taken to dryness. The residue was dissolved in ethanol and the solution was refluxed for 1.5 h. After concentration the crude product containing the benzylamine (**36**) was dissolved in a mixture of methanol and formic acid (4%) (220 ml) and reduced at room temperature in the presence of palladium black (3 g) in a stirred solution for 48 h at room temperature. After the usual work-up the crude product containing the amine (**37**) was treated with ethyl chloroformate (3.5 ml) as described before for the preparation of compound (**23**), and after purification by column chromatography (hexane–ethyl acetate, 86:14) of the extract, carbamate (**32**) (13 g) was obtained.

(20S)-20-*Ethoxycarbonyl*(*nitro*)*amino*-5α-*pregnan*-3β-*yl Acetate* (**33**).—Carbamate (**32**) (1.58 g) was dissolved in the minimum volume of glacial acetic acid and the solution was treated with conc. nitric acid–acetic anhydride (14.5:1) (25.2 ml) as described for the preparation of compound (**30**). After purification by column chromatography (hexane–ethyl acetate, 90:10), *nitrocarbamate* (**33**) (0.84 g) was obtained, m.p. 114—116 °C (from methanol); $[\alpha]_D$ −20.8° (*c* 0.24); $\nu_{max.}$ 1 730 (CO) and 1 570 cm^{-1} (NNO_2); δ_H(200 MHz) 0.73 (3 H, s, 13-Me), 0.83 (3 H, s, 10-Me), 1.34 (3 H, d, *J* 7 Hz, 20-Me), 1.40 (3 H, t, *J* 6.6 Hz, CO_2CH_2Me), 2.02 (3 H, s, $MeCO_2$), 4.36 (2 H, q, *J* 7.1 Hz, CO_2CH_2Me), and 4.68 (2 H, m, $w_{\frac{1}{2}}$ 35 Hz, 3- and 20-H); δ_C (20.1 MHz) 12.19 (C-18), 12.50 (C-19), 13.99 ($NHCO_2CH_2CH_3$), 18.50 (C-20), 21.09 (C-11), 21.33 (CH_3CO), 23.85 (C-15), 26.12 (C-12), 27.47 (C-2), 28.51 (C-6), 31.65 (C-7), 34.02 (C-4), 35.49 (C-8), 35.49 (C-10), 36.78 (C-1), 39.23 (C-16), 42.31 (C-13), 44.68 (C-5), 53.68 (C-9), 54.14 (C-17), 56.18 (C-14), 60.29 (C-20), 64.33 ($NHCO_2CH_2Me$), 73.61 (C-3), 151.53 ($NHCO_2Et$), and 170.49 (CH_3CO); *m/z* 432.3110 ($M^+ - NO_2$, 2.3%. $C_{26}H_{42}NO_4$ requires *m/z*, 432.3112), 418.2900 (4.4. $C_{25}H_{40}NO_4$ requires

m/z, 418.2955), and 344.2636 (8.6. $C_{22}H_{34}NO_2$ requires *m/z*, 344.2587).

(20S)-20-*Nitroamino*-5α-*pregnan*-3β-*yl Acetate* (**34**).—To a solution of nitrocarbamate (**33**) (1.37 g) in the smallest volume of ethanol, cooled to 0 °C, was added ammonium hydroxide (3 ml) and then the mixture was stirred at room temperature for 18 h. After this time the mixture was poured into water, acidified to pH 7 with HCl, and extracted as usual. After purification of the residue by column chromatography (benzene–ethyl acetate, 97:3), *nitroamine* (**34**) (585 mg) was obtained, m.p. 172—174 °C (from methanol); $[\alpha]_D$ +29.3° (*c* 0.28); $\nu_{max.}$ 3 390 (NH), 1 720 (CO), and 1 570 cm^{-1} (NNO_2); δ_H(200 MHz) 0.74 (3 H, s, 13-Me), 0.84 (3 H, s, 10-Me), 1.27 (3 H, d, *J* 6.3 Hz, 20-Me), 2.06 (3 H, s, $MeCO_2$), 4.15 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, 20-H), and 4.68 (1 H, m, $w_{\frac{1}{2}}$ 29 Hz, 3-H), δ_C (20.1 MHz) 12.18 (C-18), 12.28 (C-19), 19.22 (C-21), 21.03 (C-11), 21.35 (CH_3CO), 24.0 (C-15), 26.60 (C-12), 27.43 (C-2), 28.48 (C-6), 31.69 (C-7), 34.0 (C-4), 35.35 (C-8), 35.53 (C-10), 36.63 (C-1), 39.30 (C-16), 42.33 (C-13), 44.80 (C-5), 54.29 (C-9), 54.29 (C-17), 56.05 (C-20), 56.37 (C-14), 73.61 (C-3), and 170.96 (MeCO); *m/z* 360.2860 ($M^+ - NO_2$, 2%. $C_{23}H_{38}NO_2$ requires *m/z*, 360.2902), 344.2701 ($M - NH_2NO_2$, 4. $C_{23}H_{36}O_2$ requires *m/z*, 344.2715), and 269.2259 (2.5. $C_{20}H_{29}$ requires *m/z*, 269.2269).

Cyclization of (20S)-20-*Nitroamino*-5α-*pregnan*-3β-*yl Acetate* (**34**).—*Method A*. A stirred mixture of nitroamine (**34**) (100 mg, 0.25 mmol) in dry dichloromethane (10 ml), yellow HgO (200 mg, 0.92 mmol), and iodine (200 mg, 0.79 mmol) was irradiated with two 150 W tungsten-filament lamps, under Ar at 40 °C, for 2.5 h. After work-up, the residue from the organic extracts was purified by Chromatotron (benzene–ethyl acetate, 97:3) to give the starting material (15 mg, 15% recovery), and two products: (20S)-N-*nitro*-18,20-*epimino*-5α-*pregnane*-3β,18-*diol* 3-*acetate* (**41**) (25 mg, 25%), and (20S)-18-*iodo*-20-*nitroamino*-5α-*pregnan*-3β-*yl acetate* (**39**) (30 mg, 23%).

Compound (**41**) had m.p. 255—257 °C (from acetone–pentane); $[\alpha]_D$ +43.7° (*c* 0.32); $\nu_{max.}$ 3 560 (OH), 1 710 (OAc), and 1 510 cm^{-1} (NNO_2); δ_H(200 MHz) 0.83 (3 H, s, 10-Me), 1.48 (3 H, d, *J* 6.2 Hz, 20-Me), 2.02 (3 H, s, $MeCO_2$), 417 (1 H, m, *J* 6.1 Hz, 20-H), 4.69 (1 H, m, $w_{\frac{1}{2}}$ 25 Hz, 3-H), and 5.51 (1 H, s, 18-H); δ_C(20.1 MHz) 12.40 (C-19), 15.18 (C-21), 21.32 (CH_3CO), 22.12 (C-11), 24.31 (C-4), 25.91 (C-15), 27.44 (C-6), 28.37 (C-2), 32.10 (C-12), 34.0 (C-7), 35.06 (C-16), 35.67 (C-10), 36.20 (C-8), 36.66 (C-1), 44.81 (C-5), 52.44 (C-9), 52.66 (C-13), 54.58 (C-17), 55.10 (C-14), 57.93 (C-20), 73.54 (C-3), 92.21 (C-18), and 170.56 (MeCO); *m/z* 374.2660 ($M^+ - NO_2$, 3.2%. $C_{23}H_{36}ON_3$ requires *m/z*, 374.2694), 360.2705 (4. $C_{23}H_{36}O_3$ requires *m/z*, 360.2663), 342.2427 (1. $C_{22}H_{32}NO_2$ requires *m/z*, 342.2431), and 329.2360 (13. $C_{21}H_{31}NO_2$ requires *m/z*, 329.2353).

Compound (**39**) had m.p. 181—183 °C (from acetone–pentane); $[\alpha]_D$ +38° (*c* 0.2); $\nu_{max.}$ 3 400 (NH), 1 720 (CO), and 1 580 cm^{-1} (NNO_2); δ_H(200 MHz) 0.83 (3 H, s, 10-Me), 1.42 (3 H, d, *J* 6.2 Hz, 20-Me), 2.0 (3 H, s, $MeCO_2$), 3.17 and 3.30 (2 H, AB_q, *J* 11.1 Hz, 18-H_2), 4.63 (2 H, m, $w_{\frac{1}{2}}$ 40 Hz, 3-and 20-H), and 8.60 (1 H, d, *J* 7.9 Hz, NH); δ_C (20.1 MHz) 8.43 (C-18), 12.20 (C-19), 20.33 (C-21), 20.73 (C-11), 21.36 (CH_3CO), 23.69 (C-15), 25.67 (C-12), 27.42 (C-2), 28.37 (C-6), 31.66 (C-7), 33.93 (C-4), 35.52 (C-10), 36.11 (C-8), 36.71 (C-1), 39.76 (C-16), 43.70 (C-13), 44.71 (C-5), 53.99 (C-9), 54.16 (C-17), 55.76 (C-20), 56.52 (C-14), 73.56 (C-3), and 170.61 (MeCO); *m/z* 486.1887 ($M^+ - NO_2$, 2%. $C_{23}H_{37}INO_2$ requires *m/z*, 486.1869), 411.1634 (10. $C_{21}H_{32}I$ requires *m/z*, 411.1549), 359.2728 (20. $C_{23}H_{37}NO_2$ requires *m/z*, 359.2822), and 344.2581 (34. $C_{22}H_{34}NO_2$ requires *m/z*, 344. 2587).

Method B. A mixture of nitroamine (**34**) (200 mg, 0.49 mmol) in dry dichloromethane (17 ml), DIB (234 mg, 0.73 mmol), and iodine (64 mg, 0.25 mmol) was stirred, under argon, at room temperature for 7 h. After usual work-up, chromatography of the crude product (hexane–ethyl acetate, 96:4) yielded four products: (20S)-N-*nitro*-18-*oxo*-18,20-epimino-5α-*pregnan*-3β-*yl acetate* (**42**) (40 mg), the C-18 epimers of (20S)-N-*nitro*-18,20-*epimino*-5α-*pregnane*-3β,18-*diol diacetate* (**43**) (26 mg) and (**44**) (10 mg), and the hydroxy epimine (**41**) (20 mg).

Compound (**42**), m.p. 195—196 °C (from pentane–acetone); $[\alpha]_D$ +114° (*c* 0.2); $\nu_{max.}$ 1 740 (CO), 1 710 (OAc), and 1 550 cm^{-1} (NNO_2); δ_H(200 MHz) 0.90 (3 H, s, 10-Me), 1.46 (3 H, d, *J* 6.2 Hz, 20-Me), 2.02 (3 H, s, $MeCO_2$), 4.39 (1 H, m, *J* 6 Hz, 20-H), and 4.69 (1 H, m, $w_{\frac{1}{2}}$ 25 Hz, 3-H); δ_C (20.1 MHz) 12.21 (C-19), 14.97 (C-21), 20.44 (C-11), 21.39 (CH_3CO), 23.21 (C-4), 27.01 (C-15), 27.43 (C-6), 28.30 (C-2), 32.01 (C-16), 32.21 (C-12), 33.98 (C-7), 34.06 (C-8), 35.74 (C-10), 36.99 (C-1), 44.77 (C-5), 44.77 (C-17), 53.59 (C-9), 53.79 (C-13), 55.34 (C-14), 55.40 (C-20), 73.57 (C-3), 170.65 (MeCO), and 171.91 (C-18); *m/z* 401.2428 ($M^+ - OH$, 0.2%). $C_{23}H_{33}N_2O_4$ requires *m/z*, 401.2440), 371.2471 (8. $C_{23}H_{33}NO_3$ requires *m/z*, 371.2461), and 358.2408 (3. $C_{22}H_{32}NO_3$ requires *m/z*, 358.2382). Ketone (**42**) was also obtained by oxidation of the hydroxy epimine (**41**) (14 mg) with PCC (50 mg) in dry dichloromethane (5 ml), at room temperature for 4 days.

Compound (**43**), the less polar, 18*S* epimer, had m.p. 206—208 °C (from pentane–acetone); $[\alpha]_D$ +51.2° (*c* 0.16); $\nu_{max.}$ 1 740, 1 710, and 1 520 cm^{-1} (NNO_2); δ_H (200 MHz) 0.72 (3 H, s, 10-Me), 1.48 (3 H, d, *J* 6.2 Hz, 20-Me), 2.0 (3 H, s, $MeCO_2$), 2.05 (3 H, s, $MeCO_2$), 4.21 (1 H, m, *J* 5.5 Hz, 20-H), 4.66 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, 3-H), and 6.59 (1 H, s, 18-H); δ_C (20.1 MHz) 12.16 (C-19), 16.0 (C-21), 20.43 (CH_3CO), 21.32 (CH_3CO), 22.23 (C-11), 23.66 (4-C), 25.32 (C-15), 27.30 (C-6), 28.04 (C-2), 31.94 (C-12), 32.23 (C-7), 33.86 (C-16), 35.47 (C-10), 35.72 (C-8), 36.79 (C-1), 44.62 (C-5), 51.98 (C-13), 52.08 (C-9), 53.67 (C-17), 55.96 (C-14), 58.31 (C-20), 73.49 (C-3), 85.16 (C-18), 166.95 (CH_3CO), and 170.59 (CH_3CO); *m/z* 403.2594 ($M^+ - CH_3CO_2$, 4%). $C_{23}H_{35}N_2O_4$ requires *m/z*, 403.2597), 374.2676 (63. $C_{23}H_{36}NO_3$ requires *m/z*, 374.2695), and 269.2252 (80. $C_{20}H_{29}$ requires *m/z*, 269.2268).

The more polar, 18*R* epimer (**44**) had m.p. 181—183 °C (from pentane–acetone); $\nu_{max.}$ 1 740, 1 710 (OAc) and 1 520 cm^{-1} (NNO_2); δ_H(200 MHz) 0.82 (3 H, s, 10-Me), 1.50 (3 H, d, *J* 6.2 Hz, 20-Me), 2.02 (3 H, s, $MeCO_2$), 2.10 (3 H, s, $MeCO_2$), 4.27 (1 H, m, *J* 6.2 Hz, 20-H), 4.68 (1 H, m, $w_{\frac{1}{2}}$ 26 Hz, 3-H), and 6.87 (1 H, s, 18-H); *m/z* 403.2554 ($M^+ - CH_3CO_2$, 7%. $C_{23}H_{35}N_2O_4$ requires *m/z*, 403.2594), 374.2680 (20. $C_{23}H_{36}NO_3$ requires (*m/z*, 374. 2693), 329,2310 (56. $C_{21}H_{31}NO_2$ requires *m/z*, 329.2343), and 269.2186 (69. $C_{20}H_{29}$ requires *m/z*, 269.2267).

(20S)-N-*Nitro*-18,20-*epimino*-5α-*pregnan*-3β-*yl Acetate* (**45**).—A mixture of iodonitroamine (**39**) (90 mg) in dry diethyl ether (30 ml) and silver acetate (150 mg) was stirred, under Ar at room temperature, for 24 h. After usual work-up the organic extract was purified by Chromatotron (hexane–ethyl acetate, 96:4) to yield the *imino compound* (**45**) (44 mg, 65%), m.p. 185—186 °C (from methanol); $[\alpha]_D$ +73.5° (*c* 0.26); $\nu_{max.}$ 1 710 (OAc) and 1 490 cm^{-1} (NNO_2); δ_H (200 MHz) 0.79 (3 H, s, 10-Me), 1.45 (3 H, d, *J* 6.2 Hz, 20-Me), 2.02 (3 H, s, $MeCO_2$), 3.47 and 3.92 (2 H, ABq, *J* 12.8 Hz, 18-H_2), 4.29 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, 20-H), and 4.68 (1 H, m, $w_{\frac{1}{2}}$ 30 Hz, 3-H); δ_C(50.3 MHz) 12.40 (C-19), 15.54 (C-21), 21.53 (CH_3CO_2), 22.04 (C-4), 22.89 (C-11), 24.90 (C-15), 27.50 (C-6), 28.26 (C-2), 30.0 (C-13), 32.1 (C-12), 34.02 (C-7), 34.28 (C-16), 35.67 (C-10), 36.91 (C-1), 38.24 (C-8). 44.67 (C-5), 50.73 (C-9), 52.87 (C-14), 53.70 (C-17), 53.74 (C-18), 59.73 (C-20), 73.56 (C-3), and 170.76 (CO); *m/z* 358.2701 ($M^+ - NO_2$, 66%. $C_{23}H_{36}NO_2$ requires *m/z*, 358.2743) and 344.2480 ($M - CH_3CO_2H$, 29. $C_{21}H_{32}N_2O_2$ requires *m/z*, 344.2462).

Cyclization of (23R,25S)-3β-*Acetoxy*-23-*nitroamino*-5β-*spirostan** (**46**).—A mixture of nitroamine (**46**) (90 mg, 0.17 mmol), iodine (60 mg, 0.24 mmol), and LTA (30 mg, 0.7 mmol) in cyclohexane (30 ml) was heated at 60 °C for 2.5 h under irradiation as described above. Then the reaction mixture was worked up as usual and, after concentration of the extract, the crude product was purified by chromatography by Chromatotron (hexane–ethyl acetate, 85:15 and then ethyl acetate) to give the *imino compound* (**48**) (23 mg) and a polar compound (50 mg), which was methylated with CH_2N_2 to give the *methyl ester* (**47**).

Epimine (**48**) had m.p. 276—278 °C (from acetone); $[\alpha]_D$ −13° (*c* 0.22); $\nu_{max.}$ 1 720 (CO) and 1 490 cm^{-1} (NNO_2); δ_H(200 MHz) 0.81 (3 H, s, 13-Me), 0.91 (3 H, d, *J* 7 Hz, 20-Me), 0.99 (3 H, s, 10-Me), 2.0 (3 H, s, $MeCO_2$), 3.55—3.93 (4 H, 26- and 27-H_2), 4.48 (1 H, m, $w_{\frac{1}{2}}$ 15 Hz, 16-H), 4.76 (1 H, m, $w_{\frac{1}{2}}$ 10 Hz, 23-H), and 5.06 (1 H, m, $w_{\frac{1}{2}}$ 10 Hz, 3-H); *m/z* 517 (c.i. M^+ + 1), 470.3231 (*M* − NO_2, 100%. $C_{29}H_{44}NO_4$ requires *m/z*, 470.3270), 440.3149 (3. $C_{28}H_{42}NO_3$ requires *m/z*, 440.3164), 410.3041 (12. $C_{27}H_{40}NO_2$ requires *m/z*, 410.3059), 389.2675 (7. $C_{24}H_{37}O_4$ requires *m/z*, 389.2692), and 329.2491 (30. $C_{22}H_{33}O_2$ requires *m/z*, 329.2486).

Methyl ester (**47**) had m.p. 195—197 °C (from acetone); $[\alpha]_D$ −132° (*c* 0.12); $\nu_{max.}$ 1 720 (CO) and 1 550 cm^{-1} [N=N(O)OMe]; δ_H(200 MHz) 0.72 (3 H, s, 13-Me), 0.97 (3 H, s, 19-Me), 1.06 (3 H, d, *J* 7 Hz, 20-Me), 2.04 (3 H, s, $MeCO_2$), 3.68 (3 H, s, MeO), 3.94 [3 H, s, N=N(O)OMe], 3.7 (1 H, m, 23-H), 4.23 and 3.99 (2 H, *AB*X, *J* 11.2 and 3.4 Hz, 26-H_2), 4.48 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, 16-H), and 5.05 (1 H, m, $W_{\frac{1}{2}}$ 10 Hz, 3-H); *m/z* 530.3512 (M^+ − NO_2, 1%. $C_{31}H_{48}NO_6$ requires *m/z*, 530.3481), 515.3220 (2. $C_{30}H_{45}NO_6$ requires *m/z*, 515.3246), and 500.3143 (100. $C_{30}H_{44}O_6$ requires *m/z*, 500.3137).

Methyl 3β-*Nitroaminofriedelan*-29-*oate* (**54**).—To a combination of oxime (**50** {m.p. 240—242 °C (from chloroform–methanol); $[\alpha]_D$ +56° (*c* 0.254); $\nu_{max.}$ 3 280 (OH) and 1 720 cm^{-1} (CO); δ_H(200 MHz) 0.73, 0.83, 0.96, 0.99, 1.00, and 1.22 (18 H, 6 s, 5-, 9-, 13-, 14-, 17-, and 20-Me), 0.93 (3 H, d, *J* 6.8 Hz, 4-Me), 3.68 (3 H, s, CO_2Me), and 7.85 (1 H, m, $w_{\frac{1}{2}}$ 10.5 Hz, NOH); *m/z* 485 (M^+, 44%), 469 (77), 468 (55), 454 (100), 452 (15), and 385 (18)} (200 mg) in dichloromethane (15 ml) and sodium nitrite (170 mg) was added dropwise a mixture of glacial acetic acid (0.7 ml) and dichloromethane (1.5 ml) during 1 h. The reaction mixture was kept at room temperature for 3 h and then poured into water and worked up as usual. The crude product containing the nitroimine (**52**) was dissolved in ethanol (40 ml) and reduced with an excess of sodium borohydride (200 mg) as described for the synthesis of nitroamine (**4**). After work-up the residue was purified by chromatography (benzene–ethyl acetate, 98:2), to give the *title compound* (**54**) (153 mg), m.p. 202—204 °C (from acetone); $[\alpha]_D$ +61° (*c* 0.23); $\nu_{max.}$ 3 400 (NH), 1 720 (CO), and 1 570 cm^{-1} (NNO_2); δ_H (200 MHz) 0.81, 0.88, 0.95, 0.92 (2 ×), and 1.22 (18 H, 5 × s, 5-, 9-, 13-, 14-, 17-, and 20-Me), 0.92 (3 H, d, *J* 6.2, 4-Me), 3.68 (3 H, s, CO_2Me), 4.24 (1 H, m, $w_{\frac{1}{2}}$ 15.8 Hz, 3-H), and 8.45 (1 H, m, $w_{\frac{1}{2}}$ 21 Hz, $NHNO_2$); *m/z* 516.3931 (M^+, 5%. $C_{31}H_{52}N_2O_4$ requires *M*, 516.3927), 501.3632 (*M* − CH_3, 2. $C_{30}H_{49}N_2O_4$ requires *m/z*, 501.3692), 470.3854 (*M* − NO_2, 21. $C_{31}H_{52}NO_2$ requires *m/z*, 470. 3998), 454.3773 (*M* − NH_2NO_2, 42. $C_{31}H_{50}O_2$ requires *m/z*, 454.3810), 386.3175 (20. $C_{26}H_{42}O_2$ requires *m/z*, 386.3185), 262.1957 (100. $C_{17}H_{26}O_2$ requires *m/z*, 262.1933), 249.1827 (45. $C_{16}H_{25}O_2$ requires *m/z*, 249.1854), and 169.1216 (69. $C_{10}H_{17}O_2$ requires *m/z*, 169.1229).

* *Editor's note:* The stereochemical *sequence-rule prefix* for C-22 is *S*, although the *configuration* at C-22 is the same as in the parent (22*R*, 25*S*)-spirostan. See steroid rule 25—3.3, *Pure Appl. Chem.*, 1972, **31**, 299, lines 3 and 4: we have taken 'configurations' to read 'configurations *but not configurational prefixes*.'

Methyl N-*Nitro*-3β,24-*epiminofriedelan*-29-*oate* (**57**) *and Methyl* 25-*Iodo*-N-*nitro*-3β,24-*epiminofriedelan*-29-*oate* (**58**).—A mixture of nitroamine (**54**) (109 mg, 0.21 mmol), iodine (80 mg, 0.31 mmol), and LTA (290 mg, 0.65 mmol) in cyclohexane–dichloromethane (6:1) (35 ml) was irradiated at 40—50 °C with two 150 W tungsten-filament lamps for 1.5 h. Then the reaction mixture was poured into water and worked up as usual. After concentration the extract was purified by column chromatography (benzene–ethyl acetate, 99:1) to give a two-component mixture, which was separated by rotative chromatography (hexane–ethyl acetate, 95:5) to yield *imino compound* (**57**) (55 mg) and the *iodo epimine* (**58**) (19 mg).

Compound (**57**) had m.p. 260—262 °C (from acetone–pentane); $[\alpha]_D$ +75° (*c* 0.21); $\nu_{max.}$ 1 715 (CO) and 1 490 cm^{-1} (NNO_2); δ_H (200 MHz) 0.94, 0.95, 0.98 (2 ×), and 1.21 (15 H, 4 × s, 9-, 13-, 14-, 17-, and 20-Me), 0.90 (3 H, d, *J* 6.6 Hz, 4-Me), 3.68 (3 H, s, CO_2Me), 3.44 and 4.27 (2 H, ABq, *J* 12.4 Hz, 24-H_2), and 4.23 (1 H, d, *J* 3.4 Hz, 3-H); *m/z* 514.3861 (M^+, 3%. $C_{31}H_{50}N_2O_4$ requires *M*, 514.3767), 497.3887 (17. $C_{31}H_{49}N_2O_3$ requires *m/z*, 497.3742), 468.3916 (*M* − NO_2, 38. $C_{31}H_{50}NO_2$ requires *m/z*, 468.3845), 385.3135 (6. $C_{26}H_{41}O_2$ requires *m/z*, 385.3105), 317.2242 (14. $C_{19}H_{29}N_2O_2$ requires *m/z*, 317.2227), 271.2286 (20. $C_{19}H_{29}N$ requires *m/z*, 271.2298), 249.1818 (20. $C_{16}H_{25}O_2$ requires *m/z*, 249.1852), and 169.1191 (100. $C_{10}H_{17}O_2$ requires *m/z*, 169.1228).

Iodo epimine (**58**) had m.p. 193—196 °C (from chloroform–methanol); $[\alpha]_D$ +16° (*c* 0.13); $\nu_{max.}$ 1 720 (CO) and 1 490 cm^{-1} (NNO_2); δ_H(200 MHz) 0.99, 1.01, 1.03, and 1.22 (12 H, 4 xs, 13-, 14-, 17-, and 20-Me), 0.95 (3 H, d, *J* 7 Hz, 4-Me), 3.69 (3 H, s, CO_2Me), 3.45 and 3.87 (2 H, ABq, *J* 11.8 Hz, 25-H_2), 3.59 and 4.30 (2 H, ABq, *J* 12.4 Hz, 24-H_2), and 4.25 (1 H, d, *J* 3.8 Hz, 3-H); *m/z* 512.3610 (*M*$^+$ − HI, 3%, $C_{31}H_{48}N_2O_4$ requires *m/z*, 512.3612), 495.3163 (8. $C_{31}H_{45}NO_4$ requires *m/z*, 495.3345), 466.3661 (100. $C_{31}H_{48}NO_2$ requires *m/z*, 466.3684), 315.1909 (3. $C_{19}H_{27}N_2O_2$, requires *m/z*, 315.1993), 298.2645 (4. $C_{21}H_{32}N$ requires *m/z*, 298.2534), 249.1879 (49. $C_{16}H_{25}O_2$ requires *m/z*, 249.1853), and 169.1150 (27. $C_{10}H_{17}O_2$ requires *m/z*, 169.1227).

3β-*Nitroaminofriedelane* (**53**).—A solution of oxime (**49**) {m.p. 290—292 °C (from ethyl acetate); $[\alpha]_D$ +56° (*c* 0.26); $\nu_{max.}$ 3 580 cm^{-1} (OH); δ_H(200 MHz) 0.74, 0.84, 0.95, 0.99 (2 ×), 1.03, and 1.17 (21 H, 6 × s, 5-, 9-, 13-, 14-, and 17-Me, and 20-Me_2) and 0.93 (3 H, d, *J* 6.4 Hz, 4-Me); *m/z* 441 (M^+, 6%), 425 (52), 424 (21), 423 (15), 410 (100), and 408 (22)} (500 mg) in dichloromethane (41 ml) was treated with sodium nitrite (471 mg), as described for the preparation of compound (**52**), to give the nitroimine (**51**), which was used in the following reaction without further purification. The crude product containing the nitroimine (**51**) (500 mg) was reduced with sodium borohydride (500 mg) as described for the synthesis of nitroamine (**54**), to give the title compound (**53**) (313 mg) after purification by column chromatography (benzene), m.p. 205—207 °C (from acetone); $[\alpha]_D$ +45.3° (*c* 0.23); $\nu_{max.}$ 3 410 (NH) and 1 570 cm^{-1} (NNO_2); δ_H(200 MHz) 0.82, 0.89, 0.94, 0.99 (3 ×), and 1.17 (21 H, 5 × s, 5-, 9-, 13-, 14-, and 17-Me, and 20-Me_2), 0.92 (3 H, d, 4-Me), 4.23 (1 H, m, $w_{\frac{1}{2}}$ 15 Hz, 3-H), and 8.48 (1 H, m, $w_{\frac{1}{2}}$ 20 Hz, $NHNO_2$); δ_C (50.3 MHz) 11.76 (C-23), 16.05 (C-24), 16.49 (C-1), 17.65 (C-7), 18.25 (C-25), 18.75 (C-26), 20.22 (C-27), 28.32 (C-20), 30.17 (C-17), 30.68 (C-12), 31.09 (C-2), 31.94 (C-30), 32.25 (C-28), 32.50 (C-15), 32.98 (C-21), 35.16 (C-29), 35.52 (C-11 and C-19) (2 s), 36.18 (C-16), 37.18 (C-9), 38.03 (C-5), 38.51 (C-13), 39.41 (C-22), 39.82 (C-14), 41.20 (C-6), 43.0 (C-18), 47.07 (C-4), 53.14 (C-8), 58.48 (C-3), and 60.93 (C-10); *m/z* 472 (M^+, 3%), 457 (*M* − CH_3, 3), 426 (*M* − NO_2, 4), 410 (*M* − NH_2NO_2, 11), and 395 (9).

N-*Nitro*-3β,24-*epiminofriedelane* (**55**) *and* 25-*Iodo*-N-*nitro*-3β,24-*epiminofriedelane* (**56**).—A mixture of nitroamine (**53**) (65

mg, 0.14 mmol), iodine (60 mg, 0.24 mmol), and LTA (200 mg, 0.45 mmol) in cyclohexane–dichloromethane (6:1) (35 ml) was irradiated at 55—65 °C as described previously for 1 h. After usual work-up and purification by rotative chromatography (hexane–ethyl acetate, 98:2) two products were obtained, the *imino compound* (**55**) (15 mg) and the *iodo epimine* (**56**) (34 mg).

Compound (**55**) had m.p. >300 °C (from chloroform–methanol): $[\alpha]_D$ +56° (*c* 0.22); $\nu_{max.}$ 1 480 cm^{-1} (NNO_2); δ_H(200 MHz) 0.94, 0.95, 0.99 (2 ×), 1.00, and 1.16 (18 H, 5 × s, 9-, 13-, 14-, and 17-Me, and 20-Me_2), 0.93 (3 H, d, *J* 7 Hz, 4-Me), 3.45 and 4.27 (2 H, ABq, *J* 12.5 Hz, 24-H_2), and 4.23 (1 H, d, *J* 3.9 Hz); δ_C(50.3 MHz) 13.58 (C-23), 16.73 (C-25), 18.74 (C-26 and C-1) (2 s), 19.52 (C-7), 20.66 (C-27), 27.77 (C-2), 28.30 (C-20), 30.14 (C-17), 30.24 (C-12), 31.96 (C-30), 32.28 (C-28), 32.77 (C-15), 32.96 (C-21), 34.90 (C-6), 35.13 (C-11), 35.13 (C-29), 35.46 (C-19), 36.11 (C-16), 37.59 (C-9), 38.32 (C-13), 39.39 (C-22), 39.73 (C-14), 42.90 (C-18), 44.72 (C-5), 50.69 (C-4), 52.87 (C-8), 55.74 (C-24), 57.53 (C-10), 65.91 (C-3); *m/z* 470.3910 (M^+, 3%. $C_{30}H_{50}N_2O_2$ requires *M*, 470.3870), 455.3661 ($M - CH_3$, 5. $C_{29}H_{47}N_2O_2$ requires *m/z*, 455.3635), 424.3932 ($M - NO_2$, 21. $C_{30}H_{50}N$ requires *m/z*, 424.3923), 346.2640 (30. $C_{21}H_{34}N_2O_2$ requires *m/z*, 346.2618), 317.2211 (17. $C_{19}H_{29}N_2O_2$ requires *m/z*, 317.2195), 205. 1919 (51. $C_{15}H_{25}$ requires *m/z*, 205.1883), and 109.1035 (100. C_8H_{13} requires *m/z* 109.1016).

Iodo compound (**56**) had m.p. 176—178 °C (from chloroform–methanol); $[\alpha]_D$ −10° (*c* 0.28); $\nu_{max.}$ 1 490 cm^{-1} (NNO_2); δ_H (200 MHz) 0.94, 0.99, 1.02, 1.06, and 1.18 (15 H, 5 × s, 13-, 14-, and 17-Me, and 20-Me_2), 0.95 (3 H, d, *J* 6.9 Hz, 4-Me), 3.48 and 3.89 (2 H, ABq, *J* 11.7 Hz, 25-H_2), 3.59 and 4.31 (2 H, ABq, *J* 12.5 Hz, 24-H_2), and 4.25 (1 H, d, *J* 3.7 Hz, 3-H); δ_C (50.3 MHz) 11.59 (C-25), 13.64 (C-23), 18.91 (C-26), 19.78 (C-7), 20.88 (C-1), 21.75 (C-27), 28.04 (C-20), 28.23 (C-2), 29.66 (C-12), 29.90 (C-17), 31.82 (C-30), 32.64 (C-15 and C-28) (2s), 32.84 (C-21), 35.28 (C-29), 35.33 (C-11), 35.48 (C-19), 35.94 (C-6), 36.03 (C-16), 38.10 (C-9 or -13), 38.61 (C-13 or -9), 39.51 (C-14), 39.60 (C-22), 42.56 (C-18), 44.65 (C-5), 51.51 (C-4), 53.21 (C-8), 56.41 (C-24), 59.17 (C-10), and 65.61 (C-3); *m/z* 468.3647 ($M^+ - HI$, 5. $C_{30}H_{48}N_2O_2$ requires *m/z*, 468.3715), 451.3838 (68. $C_{30}H_{47}N_2O$ requires *m/z*, 451.3687), 422.3722 (17. $C_{30}H_{48}N$ requires *m/z*, 422.3785), 406.3466 (23. $C_{30}H_{46}$ requires *m/z* 406.3597), 315.2065 (19. $C_{19}H_{27}N_2O_2$ requires *m/z*, 315.2070), 205.1982 (86. $C_{15}H_{25}$ requires *m/z*, 205.1955), and 123.1182 (100. C_9H_{15} requires *m/z*, 123.1173).

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