HYDROGENATION OF A TETRASUBSTITUTED DOUBLE BOND: SYNTHESIS OF 5-METHYL-19-NOR-5β-PREGNANES*

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Dedicated to Dr Jan Fajkos on the occasion of his 75th birthday.

Reduction of C=C and/or C=O bonds in 5-methyl-19-nor-5β-pregn-9-ene-3,20-dione (**1**) leads to saturated and unsaturated ketones and hydroxy ketones. The C=C reduction affords mainly 9β,10β and 9α,10β dihydro products. Reaction conditions of partial esterification, hydrolysis and oxidation were elaborated. Several analogues were prepared for the testing of gestagenic and neurosteroidal activities.

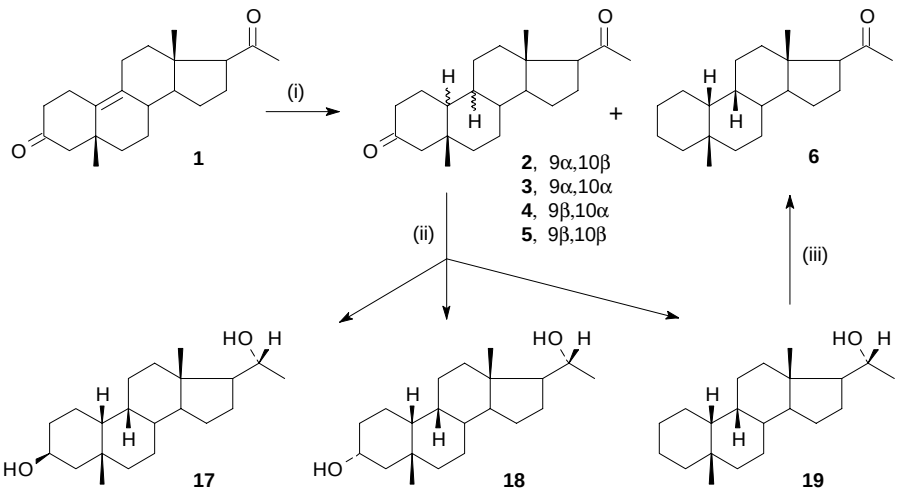
Key words: Westphalen rearrangement; Partial acetylation; Partial oxidation; Partial hydrolysis; ^{1}H NMR spectroscopy; Hydrogenolysis; Configuration; Steroids.

In our search for new analogues of steroid hormones[2,3], we prepared 5-methyl-19-nor-5β-pregn-9-en-3,20-dione[4] (**1**) which turned out to cause abortion in rats[5] and inhibited fat deposition in the breast[6]. Here we deal with further modification of this compound, consisting in the saturation of double bonds of the active compound which modifies the overall conformation of the molecule and/or changes its functional groups.

Platinum-catalyzed hydrogenation of the tetrasubstituted Δ^9-double bond was first carried out by Grob[7], who was the first to discover an apparent *trans* addition of hydrogen at the Δ^9-double bond and to explain that this resistant double bond is first isomerized by contact with the catalyst and only then hydrogenated. Snatzke[8] found a directing role in the hydrogenation of substituents in the position 6β and recently we found[9] that in the absence of 6β-substituents, a 3β-hydroxy group controls the stereochemistry of the hydrogenation.

* Part CCCXCIX in the series On Steroids; Part CCCXCVIII see ref.[1]

The resistance of the Δ^9-double bond to saturation was manifested in the hydrogenation of diketone **1** (Scheme 1) – under conditions of forced hydrogenation (acetic acid, excess of the Adams catalyst, prolonged treatment), reductive deoxygenation of an oxo group competed with the C=C saturation[10,11] – in addition of dihydro derivative **2** and

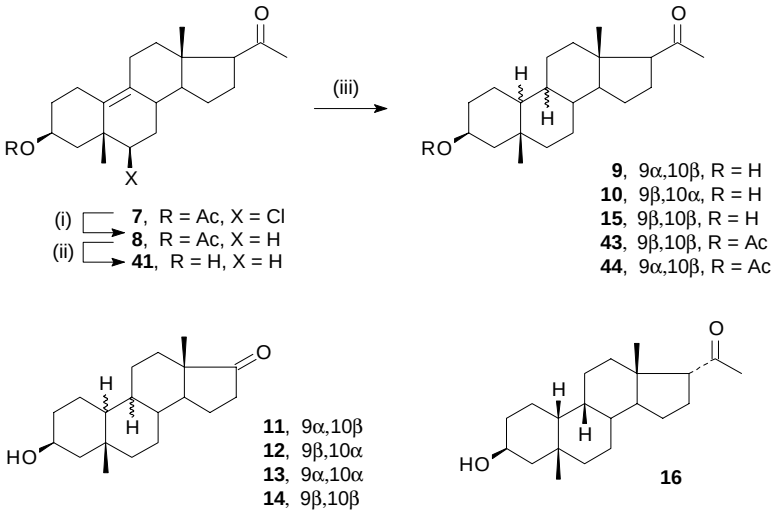


(i) 1. H_2-Pt/AcOH, 2. Jones reagent/acetone; (ii) H_2-Pt/AcOH; (iii) Jones reagent/acetone

SCHEME 1

an intractable mixture of its isomers **3**, **4** and **5**, 3-deoxy compound **6** was formed (23%). The given structures were confirmed by correlation with samples prepared as follows: 6β-chloro derivative **7** (ref.[12], Scheme 2) was treated with tributylstannane to yield compound **8**. Its hydrogenation under the same conditions afforded a mixture of perhydro derivatives that was re-oxidized to a mixture of acetoxy ketones and hydrolyzed. A lipophilic fraction of the mixture (chromatography on silica gel) was a mixture of two hydroxy ketones **9**, **10** with a hydroxy group in an axial position. Its more abundant component **9** was isolated by crystallization of the mixture: the 9α,10β structure assignment is based on a parallel with the recently studied hydrogenation of androstane homologues[9] leading to compounds **11**, **12**, **13** and **14** (see Table I).

The two most polar isomers **15** and **16** exhibited characteristics of the expected 9β,10β-dihydro derivative **15**, *i.e.* a broad signal (a triplet of triplets) of the H-3α which is axial in the 9β,10β-isomer only. Both isomers **15** and **16**, however, differ in their ^{1}H NMR spectra: an H-17 signal at δ 2.56 is a triplet in the more lipophilic isomer **15** and a doublet of doublets (δ 2.83) in the more polar one (**16**). Chemical shift of H-18 signals of the two compounds also differ significantly (δ 0.62 and δ 0.92, respectively). The given patterns correspond to C-17 isomers which was proved by circular dichroism: CD curves of the isomers differ in a way expected of 17α- and 17β-pregnan-20-ones[13].



(i) tributylstannane/benzene; (ii) MeONa, MeOH; (iii) 1. H_2-Pt/AcOH, 2. Jones reagent/acetone

SCHEME 2

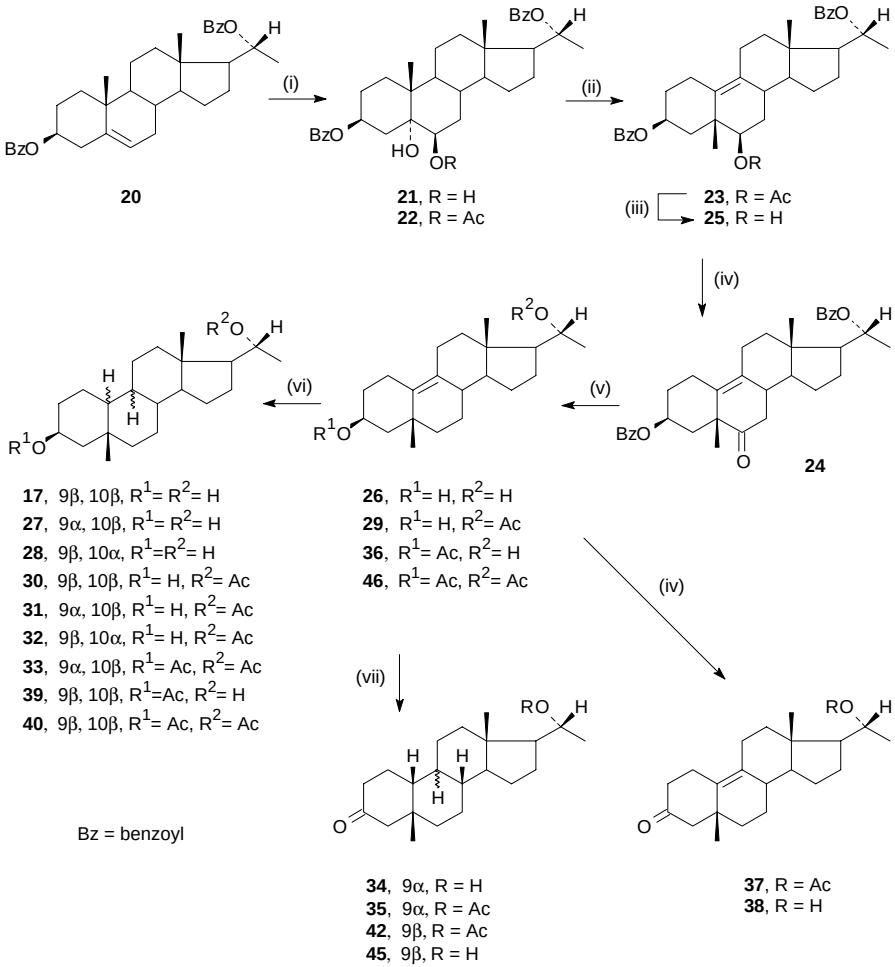
TABLE I
^{1}H NMR spectra, chemical shifts (δ-scale) as criteria for differentiation between 9,10-isomers

Compound	9,10-Configuration	H-3	C(5)-Me
13	9α,10α	4.07 m[a]	1.29 s
11	9α,10β	4.16 m[a]	1.22 s
9	9α,10β	4.16 m[a]	1.20 s
31	9α,10β	4.16 m[a]	1.19 s
12	9β,10α	4.11 m[a]	1.12 s
10	9β,10α	4.11 m[a]	1.18 s
28	9β,10α	4.11 m[a]	1.20 s
14	9β,10β	3.71 tt[b]	1.04 s
30	9β,10β	3.72 tt[b]	1.01 s
15	9β,10β	3.73 tt[b]	1.02 s
17	9β,10β	3.73 tt[b]	1.01 s

[a] W = 17.5 Hz. [b] $J(3\alpha,2\beta) = J(3\alpha,4\beta)$ = 11.6 Hz and $J(2\alpha,3\alpha) = J(3\alpha,4\alpha)$ = 4.1 Hz.

Compound **15** was oxidized to the above diketone **5**, diketone **5** was hydrogenated to afford two diols **17** and **18** (Scheme 1) and alcohol **19** which could be oxidized to the monoketone **6**: this correlation confirms the 9β,10β-configuration in compounds **5** and **6**.

Other analogues of diketone **1** were prepared from (20*R*)-pregn-5-ene-3β,20-diyl dibenzoate (**20**, Scheme 3) as follows: a buffered solution of peroxyacetic acid converted olefin **20** into a mixture of epoxides which were hydrated to 5,6-diol **21** (an



(i) 1. $AcOOH/CHCl_3$; 2. $HClO_4$/dioxane,acetone; (ii) H_2SO_4, Ac_2O; (iii) $HCl/CHCl_3$, MeOH; (iv) Jones reagent/acetone; (v) $N_2H_4.H_2O$, KOH/diethyleneglycol, 200°C; (vi) H_2-Pt/AcOH (vii) Jones reagent/acetone, -65°C

SCHEME 3

unbuffered solution of peroxyacetic acid yielded a mixture of compound **21** and its acetate **22**). Acid catalyzed dehydration of the diol produced a Westphalen-type product **23** (for ^{1}H NMR data see Table II). Deoxygenation in the position 6 was carried out by the Huang–Minlon reduction[9] of ketone **24** prepared in a routine way *via* compound **25**. Hydrogenation of diol **26** proceeded without the above complications (deoxygenation of the 3-oxo group, equilibration of the pregnane side chain) to yield diols **17**, **27** and **28**. The 9β,10β-configuration of the first isomer (**17**) is again unambiguously proved by the equatorial nature of the 3β-hydroxy group (H-3α is a triplet of triplets, J = 11.3 and 4.1 Hz). In ascribing structures **27** and **28** to the isomers, the signal of the 3α-proton was evaluated as above (see Table I). The 9α,10β compound **27** could be obtained by crystallization of the mixture.

Equally, we hydrogenated diol monoacetate **29** and obtained acetates **30** and **31** as major products. Their isomer **32** was a more polar admixture of compound **31**, crystallization again proved sufficient to produce the pure major isomer **31**.

Oxidation of diols **27** and **17** afforded diketones **2** and **5**, respectively, which were identical with the above obtained samples. The third diketone (**4**), formed in about 5% yield, was not isolated, nevertheless, its NMR signals could be detected in the mother liquor of compound **2**.

The 3β hydroxy group in the 9α,10β-pregnane derivative **27** is axial and thus its reactivity is lower than that of the C-20 hydroxyl. Compound **27** could therefore be partially acetylated to yield 20-monoacetate **31** (60%) besides diacetate **33**. Diol **27** could also be partially oxidized[14] to yield mainly hydroxy ketone **34** (58%) which was available also from 20-monoacetate **31** *via* acetoxy ketone **35**.

A similar sequence was attempted in acetylation of unsaturated diol **26**. Here, a mixture of 20- and 3-monoacetates **29** and **36** could not be separated by chromatography: fortunately, the major product – the 20-acetoxy derivative **29** – could be obtained by crystallization. Its oxidation (to **37**) and hydrolysis afforded another analogue **38**.

Reactivities of both hydroxy groups in the 9β,10β-diol **17** are similar and both monoacetates **39** and **30** were formed in comparable yields. However, reactivities of corresponding ester groupings are so different that a 20-acetoxy derivative **30** was available by partial hydrolysis of diacetate **40**.

The monoesters prepared above were converted in physiologically interesting monoketones **9**, **15**, **16**, **34**, **38**, **41** and **45**, and diketones **2** and **5** which will be used as probes for finding structural requirements of the studied activity[6]. Some of the compounds (**9**, **15**, **16**) are interesting for their potential neurosteroidal activity[15].

In summary, hydrogenation of Δ^9-olefins is best carried out with diol **26** or its ester **29** and yields mostly 9β,10β- and 9α,10β-dihydro products. For differentiation between identical groups in positions 3 and 20, partial oxidation of diols (*e.g.* **17**, **26**, **27**), partial acylation of diols (*e.g.* **17**, **26**, **27**) and partial hydrolysis of diesters (*e.g.* **40**, **46**) turned out to be the most useful.

TABLE II

Characteristic parameters of ^{1}H NMR spectra, chemical shifts in ppm (δ-scale), coupling constants (*J*) and width of multiplets (*W*) in Hz

Compound	H-3	H-20[a]	C5-Me	C13-Me	C20-Me	Other signals
1	–	–	1.02 s	0.75 s	2.13 s	
2	–	–	0.95 s	0.65 s	2.13 s	H-4β: 2.72 d (*J* = 14.3); H-17: 2.56 t (*J* = 8.9)
4	–	–	0.97 s	0.62 s	2.12 s	
5	–	–	1.10 s	0.64 s	2.11 s	H-17: 2.54 t (*J* = 8.9)
6	–	–	0.97 s	0.61 s	2.11 s	H-17: 2.57 t (*J* = 8.9)
8	5.09 m[b]	–	1.18 s	0.74 s	2.11 s	OAc: 2.07 s; H-17: 2.57 t (*J* = 8.9)
9	4.16 m[b]	–	1.20 s	0.61 s	2.11 s	H-17: 2.52 t (*J* = 8.9)
10	4.11 m[b]	–	1.18 s	0.64 s	2.13 s	H-17: 2.61 t (*J* = 8.9)
15	3.73 tt[c]	–	1.02 s	0.62 s	2.11 s	H-17: 2.56 t (*J* = 8.9)
16	3.55 tt[c]	–	0.99 s	0.92 s	2.11 s	H-17: 2.83 dd (*J* = 8.2 and 2.4)
17	3.73 tt[c]	3.73 dq	1.01 s	0.76 s	1.14 d	
18	4.07 m[b]	3.74 dq	0.96 s	0.77 s	1.13 d	
19	–	3.75 dq	0.95 s	0.76 s	1.13 d	
21	5.40 m[d]	5.12 dq	–	0.69 s	1.27 d	C10-Me: 1.20 s; H-6α: 3.56 m (*W* = 16); Bz: 8.05 m (2 H), 7.48 m (3 H)
22	5.38 m[d]	5.16 dq	–	0.70 s	1.27 d	C10-Me: 1.16 s; H-6α: 4.71 m (*W* = 16); OAc: 2.07 s; Bz: 8.05 m (2 H), 7.48 m (3 H)
23	5.38 m[b]	5.17 dq	1.32 s	0.82 s	1.27 d	H-6α: 4.81 dd (*J* = 11.6 and 4.0); OAc: 2.05 s; Bz: 8.05 m (2 H), 7.48 m (3 H)
24	5.42 m[b]	5.17 dq	1.47 s	0.80 s	1.28 d	Bz: 8.05 m (2 H), 7.48 m (3 H)
25	5.38 m[b]	5.17 dq	1.25 s	0.82 s	1.27 d	H-6α: 3.59 m (*W* = 30); Bz: 8.05 m (2 H), 7.48 m (3 H)
26	4.14 m[b]	3.77 dq	1.27 s	0.90 s	1.15 d	
27	4.15 m[b]	3.74 dq	1.20 s	0.75 s	1.14 s	
28	4.11 m[b]	3.74 dq	1.20 s	0.76 s	1.14 d	
29	4.16 m[b]	4.86 dq	1.25 s	0.75 s	1.14 d	OAc: 2.02 s
30	3.72 tt[c]	4.86 dq	1.01 s	0.64 s	1.15 d	OAc: 2.01 s

TABLE II
(*Continued*)

Compound	H-3	H-20[a]	C5-Me	C13-Me	C20-Me	Other signals
31	4.16 m[b]	4.84 dq	1.19 s	0.63 s	1.15 d	OAc: 2.02 s
33	5.08 m[b]	4.84 dq	1.10 s	0.63 s	1.15 d	2 × OAc: 2.01 s, 2.04 s
34	–	3.75 dq	0.94 s	0.71 s	1.15 d	H-4β: 2.73 d (*J* = 14.3)
35	–	4.86 dq	0.94 s	0.66 s	1.16 d	H-4β: 2.72 d (*J* = 14.3); OAc: 2.03 s
36	5.09 m[b]	3.77 dq	1.27 s	0.90 s	1.16 d	OAc: 2.08 s
37	–	4.88 dq	1.01 s	0.77 s	1.18 d	OAc: 2.03 s
38	–	3.76 dq	1.01 s	0.89 s	1.15 d	
39	4.82 tt[c]	3.74 dq	1.02 s	0.76 s	1.14 d	OAc: 2.02 s
40	4.84 tt[c]	4.84 dq	1.02 s	0.64 s	1.16 d	2 × OAc: 2.01 s, 2.03 s
41	4.13 m[b]	–	1.26 s	0.73 s	2.11 s	H-17: 2.52 t (*J* = 8.9)
42	–	4.86 dq	1.09 s	0.65 s	1.14 d	OAc: 2.01 s
43	4.84 tt[c]	–	1.04 s	0.63 s	2.12 s	H-17: 2.57 t (*J* = 8.9); OAc: 2.03 s
44	5.08 m[b]	–	1.09 s	0.61 s	2.12 s	H-17: 2.55 t (*J* = 8.9); OAc: 2.04 s
45	–	3.74 dq	1.09 s	0.77 s	1.13 d	
46	5.07 m[b]	4.86 dq	1.17 s	0.76 s	1.15 d	2 × OAc: 2.02 s, 2.06 s

[a] $J(17.20) = 10.1$ and $J(20,21) = 6.2$; [b] $W = 17.5$; [c] $J(3\alpha,2\beta) = J(3\alpha,4\beta) = 11.6$ and $J(2\alpha,3\alpha) = J(3\alpha,4\alpha) = 4.1$; [d] $W = 40$.

EXPERIMENTAL

Melting points were determined on a micro melting point apparatus Boetius (Germany) and are uncorrected. Analytical samples were dried over phosphorus pentoxide at 50 °C/100 Pa. Optical rotations were measured in chloroform and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Circular dichroism (Mark V apparatus) were measured in methanol. IR spectra of chloroform solutions (unless stated otherwise) were recorded on a Bruker IFS 88 spectrometer. Wavenumbers are given in cm^{-1}. ^{1}H NMR spectra of prepared compounds were measured on a Varian UNITY-200 (at 200 MHz) spectrometer at 23 °C in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) and width of multiplets (*W*) in Hz. Mass spectra were recorded on a VG Analytical ZAB-EQ spectrometer (energy of ionizing electrons 70 eV, ion source temperature 180–220 °C). HPLC analysis (isocratic chromatography in methanol water, 75/25 w/w) was done on a Spectra-Physics chromatograph (detection at 294 nm) using a Tessek Separon SGX C18 (10 μm, 4 × 250 mm) column. Thin-layer chromatography (TLC) was done on silica gel (ICN Biochemicals). Preparative thin-layer chromatography (PLC) was carried out on 200 × 200 mm plates coated with a 0.7 mm layer of the same material. For column chromatography silica gel 60–120 μm was used. Whenever aqueous solutions of hydrochloric acid, potassium hydrogen carbonate and potassium carbonate were used, their concentration was always 5%.

Hydrogenation of 5-Methyl-19-nor-5β-pregn-9-ene-3,20-dione (**1**)

Diketone **1** (250 mg, 0.79 mmol) was hydrogenated by stirring its solution in acetic acid (5 ml) with the Adams catalyst (160 mg) in a hydrogen atmosphere at room temperature for 20 h. The catalyst was filtered off and washed with acetic acid, the filtrate was evaporated in vacuum and the residue was oxidised with Jones reagent[14] under standard conditions. An excess reagent was reduced with a few drops of methanol. The product was precipitated on addition of the potassium hydrogen carbonate solution and extracted with ether. The extract was washed with water, dried over sodium sulfate and evaporated. The residue was chromatographed on a column of silica gel (100 g) in ligroin and ethyl acetate (9 : 1) to yield the following fractions.

Fraction A: *5-Methyl-19-nor-5*β,*9*β-*pregnan-20-one* (**6**, 45 mg, 23%), m.p. 133–134 °C (methanol), $[\alpha]_D$ +64 (*c* 1.1). IR spectrum: 1 706 (C=O); 1 385, 1 377, 1 356 (CH_3). Mass spectrum, *m/z* (%): 302 (90), 287(15), 259 (33), 244 (31), 217 (100). For $C_{21}H_{34}O$ (302.5) calculated: 83.38% C, 11.33% H; found: 83.43% C, 11.76% H.

Fraction B: A mixture of 9,10-isomers of 5-methyl-19-nor-5β-pregnane-3,20-dione (**2**, **4** and **5**, 167 mg, 67%) consisting of compound **2** (58%, HPLC), **4** (14%) and **5** (15%). Crystallization from methanol yielded *5-Methyl-19-nor-5*β,*9*α,*10*β-*pregnane-3,20-dione* (**2**, 26 mg), m.p. 193–194 °C, $[\alpha]_D$ +119 (*c* 1.2). IR spectrum: 1 700 (C=O); 1 422 (CH_2–CO). Mass spectrum (FAB), *m/z* (%): 317 (100), 299 (45), 283 (12), 273 (17), 255 (18) 315 (23). For $C_{21}H_{32}O_2$ (316.5) calculated: 79.70% C, 10.19% H; found: 80.06% C, 10.00 %H.

Repeated chromatography of the mother liquor yielded *5-methyl-19-nor-5*β,*9*β,*10*β-*pregnane-3,20-dione* (**5**, 19 mg), m.p. 127–128 °C, $[\alpha]_D$ +78 (*c* 1.0). Circular dichroism: $\Delta\varepsilon_{287}$ +3.38. IR spectrum: 1 703 (C=O); 1 419 (CH_2–CO); 1 358, 1 165 (CH_3). Mass spectrum (FAB), *m/z* (%): 317 (89), 299 (46), 273 (16), 255 (23), 215 (17). For $C_{21}H_{32}O_2$ (316.5) calculated: 79.70% C, 10.19% H; found: 79.71% C, 10.13% H.

Hydrogenation of 5-Methyl-19-nor-5β,9β,10β-pregnane-3,20-dione (**5**)

Diketone **5** (70 mg, 0.22 mmol) was treated with hydrogen as in the preceding experiment. PLC of the crude product (70 mg) yielded following fractions.

Fraction A: *(20R)-5-methyl-19-nor-5*β,*9*β,*10*β-*pregnan-20-ol* (**19**, 6 mg, 8%) which was oxidized to ketone **6** (see below).

Fraction B: a mixture of acetoxy alcohols (5 mg, 6%).

Fraction C: *(20R)-5-methyl-19-nor-5*β,*9*β,*10*β-*pregnane-3*α,*20-diol* (**18**, 41 mg, 54%), m.p. 203–204 °C (acetone–heptane), $[\alpha]_D$ –15 (*c* 0.9). IR spectrum: 3 615, 3 268 (O–H); 1 092, 1 057, 1 034 (C–O).

Fraction D: *(20R)-5-methyl-19-nor-5*β,*9*β,*10*β-*pregnane-3*β,*20-diol* (**17**, 7 mg, 9%) identical with the authentic sample.

5-Methyl-19-nor-5β,9β,10β-pregnan-20-one (**6**)

The above sample of compound **19** (6 mg, 0.02 mmol) was dissolved in acetone (1 ml) and treated with the Jones reagent at room temperature. After 10 min, methanol was added and the mixture was evaporated in vacuum. The residue was extracted with chloroform, the extract was concentrated and applied onto a thin layer of silica gel which was developed with benzene–ether (1 : 1). The major product (3.9 mg, 65%) was eluted with ether. Its IR and ^{1}H NMR spectra were found identical with compound **6** prepared by hydrogenation of diketone **1**.

5-Methyl-20-oxo-19-nor-5β-pregn-9-en-3β-yl Acetate (**8**)

A solution of chloro derivative **7** (10.0 g, 24.45 mmol) in toluene (150 ml) was added to a boiling solution of tributylstannane in benzene (1 M, 28 ml, 28 mmol). The solution was refluxed for 9 h, cooled and evaporated in vacuum. The product was purified by chromatography on silica gel (500 g, ligroin–ethyl acetate, 40 : 1). The major product is compound **8** (8.1 g, 89%) m.p. 93–94 °C (methanol), $[\alpha]_D$ +93 (*c* 1.0). IR spectrum: 1 725, 1 701 (C=O); 1 270, 1 248, 1 020 (OAc). For $C_{23}H_{34}O_3$ (358.5) calculated: 77.05% C, 9.56% H; found: 77.16% C, 9.21% H.

3β-Hydroxy-5-methyl-19-nor-5β-pregn-9-en-20-one (**41**)

Acetate **8** (342 mg, 0.95 mmol) was hydrolysed in methanol (5 ml) with a solution of sodium methoxide in methanol (0.87 M, 2 ml, 1.74 mmol) at ambient temperature under argon. After 3 days, acetic acid was added (0.5 ml), the solution was concentrated in vacuum and mixed with brine (30 ml). The precipitate was extracted with chloroform, the extract was washed with water, dried over sodium sulfate and evaporated. Product (310 mg, 89%) crystallized from ether–methanol, m.p. 143–146 °C, $[\alpha]_D$ +122 (*c* 1.2). IR spectrum: 3 615, 3 482 (O–H); 1 698 (C=O); 1 642 (C=C). For $C_{21}H_{32}O_2 \cdot 1.5\ CH_3OH$ (364.6) calculated: 74.13% C, 10.51% H; found: 74.24% C, 10.24% H.

Hydrogenation of 5-Methyl-20-oxo-19-nor-5β-pregn-9-en-3β-yl Acetate (**8**)

a) The Adams catalyst (150 mg) was added to a solution of compound **8** (231 mg, 0.64 mmol) in acetic acid (7 ml) and ethanol (3 ml) under a hydrogen atmosphere and the mixture was stirred at 60 °C for 24 h. After removal of the catalyst, the filtrate was evaporated in vacuum and oxidised by Jones reagent in acetone at 20 °C. The product was isolated in a standard way and hydrolysed by heating with potassium carbonate (500 mg) in aqueous methanol (80%, 12 ml) under argon at 65 °C. After 4 h, the mixture was diluted with brine and the precipitate was extracted with chloroform, washed with water, dried over sodium sulfate and evaporated. The residue was fractioned by PLC (benzene–ether, 3 : 1) to yield the following fractions.

Fraction A: a mixture of isomers of 3β-hydroxy-5-methyl-19-nor-5β-pregnan-20-one **9** and **10** (87 mg, 42%). Two crystallizations from heptane afforded pure *3β-hydroxy-5-methyl-19-nor-5β,9α,10β-pregnan-20-one* (**9**, 42 mg, 20%), m.p. 147–149 °C, $[\alpha]_D$ +98 (*c* 0.9). Circular dichroism: $\Delta\varepsilon_{287}$ +2.70. For $C_{21}H_{34}O_2$ (318.5) calculated: 79.19% C, 10.76% H; found: 78.92% C, 10.84% H.

Fraction B: *3β-hydroxy-5-methyl-19-nor-5β,9β,10β-pregnan-20-one* (**15**, 103 mg, 50%), $[\alpha]_D$ +69 (*c* 1.1). Circular dichroism: $\Delta\varepsilon_{287}$ +2.91. IR spectrum: 3 607, 3 463 (O–H); 1 698 (C=O); 1 066, 1 020 (C–O). For $C_{21}H_{34}O_2$ (318.5) calculated: 79.19% C, 10.76% H; found: 79.08% C, 10.81% H.

Fraction C: *3β-hydroxy-5-methyl-19-nor-5β,9β,10β,17β-pregnan-20-one* (**16**, 15 mg, 7%), m.p. 147–149 °C (heptane), $[\alpha]_D$ –98 (*c* 0.8). Circular dichroism: $\Delta\varepsilon_{286}$ –2.24. IR spectrum: 3 619, 3 500 (O–H); 1 700 (C=O); 1 475, 1 389 (CH_3). Mass spectrum (FAB), *m/z* (%): 319 (40), 301 (83), 283 (40), 257 (25), 214 (18), 81 (100). High resolution mass spectrum, *m/z*: for $C_{21}H_{35}O_2$ calculated 319.263706, found 319.268089.

b) Compound **8** (660 mg, 1.84 mmol) was hydrogenated in acetic acid (15 ml) and ethanol (5 ml) as above. Oxidation of the product was carried out as above. However hydrolysis with potassium carbonate (1.5 g) in aqueous methanol (80%, 36 ml), was carried out under argon at room temperature. After 4 days, acetic acid (1 ml) was added and the solution was concentrated in vacuum. The product was precipitated with brine and extracted with chloroform. After washing with water, the solution was applied on a thin layer of silica gel (12 PLC plates) to yield following fractions.

Fraction A: compound **9** (131 mg, 22%).

Fraction B: compound **15** (204 mg, 35%).

Fraction C: *5-methyl-20-oxo-19-nor-5*β,*9*α,*10*β-*pregnan-3*β-*yl acetate* (**44**, 96 mg, 15%), $[\alpha]_D$ +84 (*c* 1.1). IR spectrum: 1 725, 1 701 (C=O); 1 264, 1 250, 1 020 (C–O). Mass spectrum (FAB), *m/z* (%): 361 (M^+, 100), 283 (50), 257 (19), 241 (8), 215 (12). High resolution mass spectrum, *m/z*: for $C_{23}H_{37}O_3$ calculated 361.274270, found 361.265500.

5-Methyl-19-nor-5β,9β,10β-pregnane-3,20-dione (**5**)

a) Hydroxy ketone **15** (12 mg, 0.04 mmol) was oxidized with the Jones reagent as above. Product (11 mg, 92%), purified by PLC, had IR and NMR spectra identical with compound **5** prepared by hydrogenation of dione **1**.

b) Diol **17** (65 mg, 0.20 mmol) was oxidized with the Jones reagent and purified as above. Dione **5** (59 mg, 92%) was identical with the product prepared *sub a*).

5-Methyl-19-nor-5β,9α,10β-pregnane-3,20-dione (**2**)

a) Hydroxy ketone **9** (4 mg, 0.001 mmol) was oxidized as above, product had ^{1}H NMR spectrum identical with that of compound **2**.

b) On oxidation with the Jones reagent, diol **27** (3.5 mg, 0.001 mmol) afforded diketone **2** identical with the above sample.

(20*R*)-5,6β-Dihydroxy-5α-pregnane-3β,20-diyl 3,20-Dibenzoate (**21**)

a) A solution of diester **20** (64.4 g, 122.3 mmol) in chloroform (150 ml) was treated with disodium hydrogen phosphate heptahydrate (50.0 g, 186.5 mmol) and peroxyacetic acid (22% solution in water, 100 ml) under stirring at ambient temperature for 5 h. The aqueous layer was separated and extracted with chloroform, the extract was washed with water, a potassium hydrogen carbonate solution and water, and evaporated in vacuum. The residue was dissolved in dioxane (650 ml) and acetone (350 ml) and treated with perchloric acid (5%, 100 ml) under stirring at ambient temperature. After 4 h, the mixture was concentrated in vacuum to a quarter of the original volume and diluted with brine (500 ml). The precipitate was filtered off, washed with water and dissolved in chloroform. The solution was washed with water, dried over sodium sulfate and evaporated. Compound **21** (59.1 g, 89%) crystallized from toluene, m.p. 237–239 °C, $[\alpha]_D$ –49 (*c* 1.1). IR spectrum: 3 621, 3 595, 3 462 (O–H); 1 706 (C=O); 1 603, 1 451, 1 315, 1 177, 1 120, 1 070, 1 027 (arom.); 1 279 (C–O). For $C_{35}H_{44}O_6$ (560.7) calculated: 74.97% C, 7.91% H; found: 74.91% C, 7.86% H.

b) A solution of diester **20** (124 mg, 0.24 mmol) in chloroform (1 ml) and acetone (0.5 ml) was treated with peroxyacetic acid (22% solution in water, 1.0 ml) and perchloric acid (72%, 0.25 ml, 1.79 mmol) under stirring at ambient temperature. After 18 h, the mixture was diluted with chloroform and washed with water, a potassium hydrogen carbonate solution and water, dried and evaporated in vacuum. Thin layer chromatography (3 PLC plates, benzene–ether, 3 : 1) yielded compound **21** (73 mg, 55%) and a lipophilic product, acetate **22** (29 mg, 20%). IR spectrum: 3 620, 3 478 (O–H); 1 729, 1 709 (C=O); 1 603, 1 452 (arom.); 1 279 (C–O, benzoate); 1 257 (C–O, acetate).

(20*R*)-5-Methyl-19-nor-5β-pregn-9-ene-3β,6β,20-triyl 6-Acetate 3,20-Dibenzoate (**23**)

Compound **21** (64.0 g, 114.1 mmol) was dried by distillation with toluene which was then evaporated. Acetic anhydride (900 ml) was added and the mixture was heated until 100 ml of the distillate was obtained. The solution was cooled to 20 °C and sulfuric acid (45 drops) was added under stirring. The mixture was maintained at 30 °C for 30 min and then at 20 °C for 2 h. The solution was poured onto brine with ice (6 l) under stirring. After 18 h, the precipitate was filtered off, washed with a

solution of potassium hydrogen carbonate and water. The crude product was dissolved in chloroform, filtered through a column with silica gel (50 g), evaporated in vacuum and crystallised from a mixture of dichloromethane and methanol. M.p. 234–235 °C (38.1 g, 57%), $[\alpha]_D$ +146 (*c* 1.1). For $C_{37}H_{44}O_6$ (584.8) calculated: 76.00% C, 7.58% H; found: 75.92% C, 7.61% H.

(20*R*)-6β-Hydroxy-5-methyl-19-nor-5β-pregn-9-ene-3β,20-diyl 3,20-Dibenzoate (**25**)

A solution of acetate **23** (38.06 g, 65.1 mmol) in a mixture of chloroform (200 ml) and methanol (1 l) was treated with hydrochloric acid (20 ml) at 40 °C. After 48 h, the solution was concentrated in vacuum and diluted with brine (2 l). The precipitate was filtered off and washed with water. Compound **25** crystallized from dichloromethane–heptane (29.1 g, 82%), m.p. 224–225 °C, $[\alpha]_D$ +157 (*c* 1.1). IR spectrum: 3 611, 3 512 (O–H); 1 705 (C=O); 1 602, 1 451, 1 315 (arom.); 1 045, 988 (C–O). For $C_{35}H_{42}O_5$ (542.7) calculated: 77.46% C, 7.80% H; found: 77.39% C, 7.71% H.

(20*R*)-5-Methyl-19-nor-6-oxo-5β-pregn-9-ene-3β,20-diyl 3,20-Dibenzoate (**24**)

A solution of diester **25** (23.3 g, 42.7 mmol) in a mixture of acetone (200 ml) and toluene (200 ml) was treated with the Jones reagent at ambient temperature. After 50 min, the excess oxidant was reduced by methanol. The precipitate was filtered off and the filtrate was poured into a potassium hydrogen carbonate solution. The precipitate was extracted with ether, the extract was washed with water, dried and evaporated. The residue crystallized from dichloromethane–methanol. M.p. of ketone **24** (19.9 g, 86%) was 192–193 °C, $[\alpha]_D$ +27 (*c* 1.2). IR spectrum: 1 709, 1 427 (CH_2C=O); 1 603, 1 585, 1 491, 1 315, 1 117, 1 070, 1 002 (arom.); 1 279 (C–O). For $C_{35}H_{40}O_5$ (540.7) calculated: 77.75% C, 7.46% H; found: 77.68% C, 7.42% H.

(20*R*)-5-Methyl-19-nor-5β-pregn-9-ene-3β,20-diol (**26**)

Ketone **24** (3.0 g, 5.55 mmol) was heated with potassium hydroxide (5.7 g, 101.6 mmol) and hydrazine hydrate (10.0 ml, 205.6 mmol) in diethylene glycol (100 ml). When the temperature reached 140 °C, a reflux condenser was set in. After 1 h, the condenser was removed and the temperature was increased to 200 °C. The mixture was kept for 8 h at this temperature, then it was cooled and poured onto ice (300 g) with hydrochloric acid (15 ml). The precipitate of compound **26** (1.69 g, 95%) was filtered, washed with water and dried. M.p. 160–161 °C (toluene), undepressed with an admixture of an authentic sample[4], $[\alpha]_D$ +54 (*c* 1.0) (ref.[4] records 168–170 °C, +27).

Partial Acetylation of (20*R*)-5-Methyl-19-nor-5β-pregn-9-ene-3β,20-diol (**26**)

Diol **26** (1.7 g, 5.33 mmol) was treated with acetic anhydride (7.0 ml, 74.0 mmol) in toluene (26 ml) and pyridine (11 ml) at ambient temperature. After 2 h, methanol (10 ml) was added and the mixture was left overnight. The mixture was evaporated in vacuum, methanol was added (10 ml) and again evaporated. Chromatography of the residue yielded following the compounds.

*(20R)-5-Methyl-19-nor-5*β*-pregn-9-ene-3*β*,20-diyl diacetate* (**46**, 143 mg, 6.7%), $[\alpha]_D$ +44 (*c* 0.9). IR spectrum: 1 734 (C=O); 1 653 (C=C); 1 243, 1 030 (C–O). For $C_{25}H_{38}O_4$ (402.6) calculated: 74.59% C, 9.51% H; found: 74.29% C, 9.78% H;

*(20R)-3*β*-Hydroxy-5-methyl-19-nor-5*β*-pregn-9-en-20-yl acetate* (**29**, 821 mg, 43%) containing 15% of **36**. Crystallization afforded pure compound **29**, m.p. 139–140 °C (acetone–heptane), $[\alpha]_D$ +116 (*c* 1.1). IR spectrum: 3 615, 3 467 (O–H); 1 722 (C=O); 1 655 (C=C); 1 255, 1 044, 1 014 (C–O); 979 (C–OH). For $C_{23}H_{36}O_3$ (360.5) calculated: 76.62% C, 10.06% H; found: 76.69% C, 10.39% H;

Diol **26**, (799 mg, 47%) identical with starting material.

Hydrogenation of (20*R*)-5-Methyl-19-nor-5β-pregn-9-ene-3β,20-diol (**26**)

Diol **26** (4.0 g, 12.6 mmol) was hydrogenated as above, using platinum oxide (500 mg) in acetic acid (55 ml). After 18 h stirring at 60 °C, the catalyst was filtered off and the filtrate evaporated. The residue was dissolved in methanol (20 ml) and hydrolyzed by treatment with sodium methoxide in methanol (0.87 M, 20 ml, 17.4 mmol) at 60 °C for 1 h. Chromatography on silica gel (500 g) in 2% acetone in ligroin yielded the following fractions.

Fraction A: a mixture of isomers **27** and **28** (2.116 g, 53%). Crystallization from acetone–heptane gave pure *(20R)-5-methyl-19-nor-5*β,*9*α,*10*β-*pregnane-3*β,*20-diol* (**27**, 910 mg, 23%), m.p. 174–175 °C, $[\alpha]_D$ +15 (*c* 0.9). IR spectrum: 3 615, 3 348, 3 359 (O–H); 1 018 (C–OH). For $C_{21}H_{36}O_2$ (320.5) calculated: 78.70% C, 11.32% H; found: 78.59% C, 11.28% H.

Fraction B: *(20R)-5-Methyl-19-nor-5*β,*9*β,*10*β-*pregnane-3*β,*20-diol* (**17**, 1.674 mg, 42%), m.p. 208–210 °C (acetone–heptane), $[\alpha]_D$ +23 (*c* 1.0). IR spectrum: 3 609, 3 451 (O–H); 1 091 (C–OH). For $C_{21}H_{36}O_2$ (320.5) calculated: 78.70% C, 11.32% H; found: 78.65% C, 11.27% H.

Hydrogenation of (20*R*)-3β-Hydroxy-5-methyl-19-nor-5β-pregn-9-ene-20-yl Acetate (**29**)

Compound **29** (400 mg, 1.11 mmol) was hydrogenated as above, using platinum oxide (250 mg) in acetic acid (20 ml) and ethanol (10 ml). After the usual workup, following fractions were obtained.

Fraction A: mixture of compounds **31** and **32** (167 mg, 42%). Crystallization from acetone–heptane yielded *(20R)-3*β*-hydroxy-5-methyl-19-nor-5*β,*9*α,*10*β-*pregnane-20-yl acetate* (**31**, 97 mg, 24%), m.p. 159–160 °C, $[\alpha]_D$ +41 (*c* 0.9). IR spectrum: 3 615 (O–H); 1 721 (C=O); 1 259, 1 026 (C–OH). For $C_{23}H_{38}O_3$ (362.6) calculated: 76.20% C, 10.56% H; found: 76.17% C, 10.59% H;

Fraction B: *(20R)-3*β*-hydroxy-5-methyl-19-nor-5*β,*9*β,*10*β-*pregnane-20-yl acetate* (**30**, 174 mg, 43%), identical with the sample prepared in another way.

Partial Acetylation of (20*R*)-5-Methyl-19-nor-5β,9β,10β-pregnane-3β,20-diol (**17**)

Diol **17** (560 mg, 1.75 mmol) was treated with acetic anhydride (3.3 ml, 34.9 mmol) in toluene (13 ml) and pyridine (5.5 ml) at ambient temperature. After 4 h, methanol (10 ml) was added and the mixture was left overnight. The mixture was evaporated in vacuum, methanol was added (10 ml) and again evaporated. Chromatography (40 g of silica gel, toluene–ethyl acetate, 10 : 1) of the residue yielded following fractions.

Fraction A: *(20R)-5-methyl-19-nor-5*β,*9*β,*10*β-*pregnane-3*β,*20-diyl diacetate* (**40,** 148 mg, 21%), m.p. 132–134 °C (methanol), $[\alpha]_D$ +31 (*c* 1.0). IR spectrum: 1 722 (C=O); 1 378, 1 368 (CH_3); 1 257, 1 025 (C–O). For $C_{25}H_{40}O_4$ (404.6) calculated: 74.22% C, 9.97% H; found: 74.17% C, 9.92% H.

Fraction B: *(20R)-20-hydroxy-5-methyl-19-nor-5*β,*9*β,*10*β-*pregnan-3*β-*yl acetate* (**39**, 198 mg, 31%), $[\alpha]_D$ +8 (*c* 1.0). IR spectrum: 3 623, 3 536 (O–H); 1 735 (C=O); 1 363 (CH_3); 1 353, 1 249, 1 025 (C–O); 1 061 (C–OH). For $C_{23}H_{38}O_3$ (362.6) calculated: 76.20% C, 10.56% H; found: 75.93% C, 10.72% H.

Fraction C: *(20R)-3*β*-hydroxy-5-methyl-19-nor-5*β,*9*β,*10*β-*pregnan-20-yl acetate* (**30**, 210 mg, 33%), $[\alpha]_D$ +23 (*c* 1.0). IR spectrum: 3 620 (O–H); 1 730 (C=O); 1 377, 1 369 (CH_3); 1 246, 1 067 (C–O); 1 021, 1 038 (C–OH). For $C_{23}H_{38}O_3$ (362.6) calculated: 76.20% C, 10.56% H; found: 76.01% C, 10.49% H.

Fraction D: starting diol **26** (799 mg, 47%).

Partial Acetylation of *(20R)-5-Methyl-19-nor-5*β,*9*α,*10*β-*pregnane-3*β,*20-diol* (**27**)

Diol **27** (130 mg, 0.41 mmol) was treated with acetic anhydride (0.6 ml, 6.3 mmol) in toluene (2 ml) and pyridine (0.9 ml) as above. Thin layer chromatography (4 PLC plates, benzene–ether, 3 : 1) yielded following fractions.

Fraction A: *(20R)-5-methyl-19-nor-5*β,*9*α,*10*β-*pregnane-3*β,*20-diyl diacetate* (**33**, 17 mg, 10%), $[\alpha]_D$ +35 (*c* 1.0). IR spectrum: 1 722 (C=O); 1 368 (CH_3); 1 266, 1 254, 1 027, 1 020 (C–O). For $C_{25}H_{40}O_4$ (404.6) calculated: 74.22% C, 9.97% H; found: 74.09% C, 9.94% H.

Fraction B: *(20R)-3*β-*hydroxy-5-methyl-19-nor-5*α,*9*α,*10*β-*pregnan-20-yl acetate* (**31**, 89 mg, 60%), m.p. 159–160 °C (acetone–heptane), $[\alpha]_D$ +41 (*c* 1.3). IR spectrum: 3 615 (O–H); 1 721 (C=O); 1 363 (CH_3); 1 259, 1 026 (C–OH). For $C_{23}H_{38}O_3$ (362.6) calculated: 76.20% C, 10.56% H; found:, 75.19% C, 10.58% H.

Fraction C: diol **27** (36 mg, 28%) identical with starting material.

Partial Oxidation of (20*R*)-5-Methyl-19-nor-5β,9α,10β-pregnane-3β,20-diol (**27**)

A solution of diol **27** (160 mg, 0.50 mmol) in acetone (50 ml) was cooled to –65 °C and the Jones reagent (7 drops) was added under stirring. After 5 min, the temperature was allowed to rise to 20 °C. An excess oxidant was decomposed by methanol (8 ml). After 20 min, the solution was filtered, concentrated in vacuum and mixed with a potassium hydrogen carbonate solution. The precipitate was extracted with ether, washed with brine and dried over sodium sulfate. Thin layer chromatography (5 PLC plates, benzene–ether, 1 : 1) yielded following fractions.

Fraction A: *5-methyl-19-nor-5*β,*9*α,*10*β-*pregnane-3,20-dione* (**2**, 26 mg, 16%), identical with compound prepared above.

Fraction B: *3*β-*hydroxy-5-methyl-19-nor-5*β,*9*α,*10*β-*pregnan-20-one* (**9**, 3 mg, 2%), identical with compound prepared in another way.

Fraction C: *(20R)-20-hydroxy-5-methyl-19-nor-5*β,*9*α,*10*β-*pregnan-3-one* (**34**, 93 mg, 58%), m.p. 146–147 °C (acetone–heptane), $[\alpha]_D$ +22 (*c* 1.1). IR spectrum: 3 609, 3 475 (O–H); 1 704, 1 422 (CH_2C=O); 1 085 (C–OH).

Fraction D: starting diol **27** (19 mg, 12%).

(20*R*)-5-Methyl-3-oxo-19-nor-5β,9α,10β-pregnan-20-yl Acetate (**35**)

Monoacetate **31** (72 mg, 0.20 mmol) was oxidized as above. The product was purified by chromatography (1 PLC plate, benzene–ether 4 : 1) and crystallized from acetone–heptane. M.p. 167–168 °C (63 mg, 88%), $[\alpha]_D$ +58 (*c* 1.0). IR spectrum: 1 723, 1 260, 1 252, 1 236 (C–O, acetate); 1 711, 1 430, 1 422 (CH_2C=O). For $C_{23}H_{36}O_3$ (360.5) calculated: 76.62% C, 10.06% H; found: 76.51% C, 9.96% H.

(20*R*)-20-Hydroxy-5-methyl-19-nor-5β,9α,10β-pregnan-3-one (**34**)

A solution of sodium methoxide in methanol (0.87 M, 1 ml) was added to a solution of acetate **35** (93 mg, 0.26 mmol) in methanol (1 ml) and left aside under argon at ambient temperature. After 4 days, acetic acid (0.7 ml) and ethyl acetate (5 ml) was added, the solution was concentrated to a half and washed with brine and dried. The product was purified by PLC (2 plates, benzene–ether, 3 : 1). Elution of the major zone yielded compound **34** (74 mg, 90%) identical with the compound prepared by partial oxidation of diol **27**.

(20*R*)-20-Hydroxy-5-methyl-19-nor-5β,9β,10β-pregnan-3-one (**45**)

Analogously, acetate **42** (273 mg, 0.76 mmol) was hydrolyzed with sodium methoxide (0.87 M, 2 ml) under argon. Preparative thin layer chromatography (5 plates, benzene–ether 3 : 1) yielded compound **45** (220 mg, 91%), $[\alpha]_D$ –9 (*c* 1.2). IR spectrum: 3 611, 3 466 (O–H); 1 706, 1 419 (CH_2C=O); 1 096 (C–OH). Mass spectrum, *m/z* (%): 318 (M^+, 36), 300 (58), 285 (14), 271 (10), 242 (15), 231 (100), 217 (17), 213 (17). High resolution mass spectrum, *m/z*: for $C_{21}H_{34}O_2$ calculated 318.255881, found: 318.256481.

Partial Hydrolysis of (20*R*)-5-Methyl-19-nor-5β,9β,10β-pregnane-3β,20-diyl Diacetate (**40**)

A solution of diacetate **40** (204 mg, 0.50 mmol) in methanol (4.5 ml) was treated with sodium methoxide in methanol (0.87 M, 0.7 ml) at ambient temperature. After 20 h, the solution was acidified with acetic acid (0.5 ml) and evaporated. The residue was separated by PLC (4 plates, benzene–ether, 1 : 1) into two fractions.

Fraction A: *(20R)-3β-hydroxy-5-methyl-19-nor-5β,9β,10β-pregnan-20-yl acetate* (**30**, 154 mg, 84%), identical by PLC and IR spectrum with the above sample.

Fraction B: *(20R)-5-methyl-19-nor-5β,9β,10β-pregnane-3β,20-diol* (**17**, 20 mg, 12%), identical with the authentic sample.

5-Methyl-20-oxo-19-nor-5β,9β,10β-pregnan-3β-yl Acetate (**43**)

Compound **39** (110 mg, 0.30 mmol) was oxidized with the Jones reagent in acetone as above. Crude product was purified by PLC (2 plates, benzene–ether, 4 : 1) to yield compound **39** (101 mg, 92%), $[\alpha]_D$ +64 (*c* 1.0). IR spectrum: 1 718, 1 728 shoulder, 1 700 (C=O); 1 259, 1 026 (C–O). For $C_{23}H_{36}O_3$ (360.5): calculated: 76.62% C, 10.06% H; found: 76.40% C, 10.16% H.

(20*R*)-5-Methyl-3-oxo-19-nor-5β,9β,10β-pregnan-20-yl Acetate (**42**)

Analogously, compound **30** (430 mg, 1.19 mmol) was converted to ketone **42** (398 mg, 93%). M.p. 147–148 °C (acetone–heptane), $[\alpha]_D$ +31 (*c* 1.2). IR spectrum: 1 718 (C=O); 1 255, 1 043 (C–O). For $C_{23}H_{36}O_3$ (360.5) calculated: 76.62% C, 10.06% H; found: 76.59% C, 10.07% H.

3β-Hydroxy-5-methyl-19-nor-5β,9β,10β-pregnan-20-one (**15**)

A solution of acetate **43** (330 mg, 0.92 mmol) in methanol (8 ml) was treated with sodium methoxide in methanol (0.87 M, 1.1 ml) under nitrogen atmosphere at ambient temperature. After 18 h, the solution was acidified with acetic acid (0.8 ml) and evaporated. The residue was partitioned between ethyl acetate and brine, the organic layer was washed with water, dried over sodium sulfate and evaporated. PLC (7 plates, benzene–ether 10 : 1) gave pure compound **15** (263 mg, 90%), $[\alpha]_D$ +70 (*c* 1.0). Circular dichroism: $\Delta\varepsilon_{287}$ +2.91. IR spectrum: 3 607, 3 463 (O–H); 1 698 (C=O); 1 066, 1 020 (C–OH). Mass spectrum, *m/z* (%): 318 (M^+, 49), 303 (57), 300 (100), 285 (32), 233 (49), 215 (96). High resolution mass spectrum, *m/z*: for $C_{21}H_{34}O_2$ calculated 318.255881, found 318.256481.

(20*R*)-20-Hydroxy-5-methyl-19-nor-5β-pregn-9-en-3-one (**38**)

a) Diol monoacetate **29** (112 mg, 0.31 mmol) was oxidized with the Jones reagent in acetone (2 ml) as above. The crude product (37) was dissolved in methanol (3 ml) and treated with sodium methoxide in methanol (0.87M, 1 ml) at room temperature in argon atmosphere. After 3 days, the mixture was worked up and purified by PLC as in the preparation of compound **15**. The major product was hy-

droxy ketone **38** (26 mg, 26%) $[\alpha]_D$ –3 (*c* 1.0). IR spectrum: 3 607 (O–H); 1 703, 1 416 (CH_2–C=O); 1 085, 979 (C–OH). Mass spectrum, *m/z* (%): 316 (M^+, 100), 301 (21), 298 (29), 283 (35), 271 (18), 257 (23), 243 (13), 231 (25), 213 (20). For $C_{21}H_{32}O_2$ (316.5) calculated: 79.70% C, 10.19% H; found: 79.57% C, 10.25% H.

b) Diol **26** (300 mg, 0.94 mmol) was dissolved in acetone (90 ml) and cooled to –60 °C. Jones reagent[14] (12 drops) was added under stirring, after 5 min the temperature was allowed to rise to ambient temperature. After 45 min, methanol (10 ml) was added and the mixture was concentrated in vacuum to a fifth of its volume. A potassium hydrogen carbonate solution (15 ml) was added and the precipitate was extracted with chloroform, washed with water and dried over sodium sulfate. The solution was evaporated and the residue purified by PLC (7 plates, benzene–ether 1 : 1). The major product (**38**, 149 mg, 44%), identical with the above prepared sample, was obtained in addition to diol **26** (65 mg, 22%) and dione **1** (39 mg, 13%).

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