Rearrangement of 18-iodo- and 20-iodopregnanes mediated by iodosyl derivatives †

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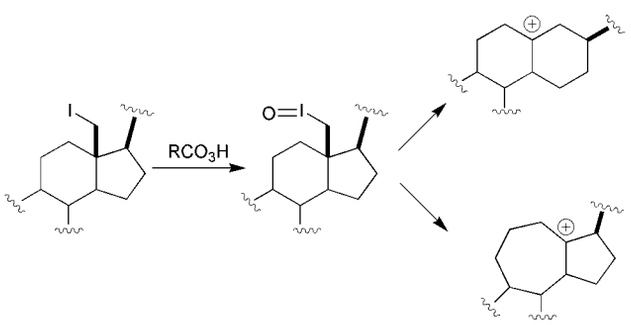
Conversion of 20-acetoxy-18-iodopregn-4-en-3-one **1** to the 18-iodosyl derivative by MCPBA resulted in a Wagner–Meerwein-type rearrangement with regioselective migration of the C13–C17 bond to give, in high yield, an *abeo*-pregnane in which C-18 was incorporated into ring D. The rearranged steroid was epoxidized *in situ* yielding a mixture of β and α 13,14-epoxides (**3** and **4**) which were characterized spectroscopically and by X-ray crystallography. When (20*R*)-20-iodopregn-4-en-3-one **9a** was used as substrate, regioselective migration of the C16–C17 bond gave the D-homoandrostane with incorporation of C-20 into ring D in up to 95% yield. The 20*S* epimer **9b** however, gave a mixture of substitution and rearrangement products. The crystal structures of the deacetylated β-epoxide **3** (**5**), the methanolysis product of α-epoxide **4** (**7**) and 20-iodopregnanes **9a** and **9b** are reported.

Introduction

The oxidation of alkyl iodides with peracids gives rise to a hypervalent iodine substituent with high nucleofugacity, which readily experiences substitutions, eliminations or rearrangements.[1] The type of reaction, as determined by product distribution, is dependent on substrate structure and solvent, thus primary iodides give mainly displacement products, although carbocationic shifts have been observed when substitution at the iodine-bearing carbon is sterically hindered (*e.g.*, treatment of neopentyl iodide with MCPBA gives only 2-methylbutan-2-ol and the corresponding *m*-chlorobenzoate).[2] In a previous publication we described the preparation of ketals and hemiketals by attack of a ketone carbonyl oxygen on a hyperelectrophilic carbon bearing the iodosyl moiety; the intermediates in these reactions, generated by MCPBA oxidation of *δ*- and γ-iodo ketones, were the cyclic oxocarbenium ions.[3] 6-Oxa-5α-pregnanes and 18-hydroxy-20-oxopregnanes (as 18,20-hemiketals) were obtained in good yields and with high stereoselectivity under mild conditions.

As a further application of iodosyl intermediates as masked carbocations we now describe their use in Wagner–Meerwein-type rearrangements using steroidal iodides as substrates. These particular Wagner–Meerwein rearrangements involve the generation of a carbocation next to a bicyclic system, followed by a 1,2-shift of an adjacent C–C bond to generate a new carbocation with modification of the bicyclic framework.[4,5] We were specially interested in the possibility of generating modified steroids with expanded rings by inclusion of C-18 into ring C or D,[6,7] under the mild reaction conditions associated with carbocation generation by peracid oxidation of an 18-iodo steroid (Scheme 1); these compounds present enhanced mobility of the steroid skeleton and often show interesting biological properties.[8]



Scheme 1

Results and discussion

As starting material we chose the readily available (20*R*)-20-acetoxy-18-iodopregn-4-en-3-one **1**. It was expected that, at variance with the 20-keto analog used previously,[3] the lower nucleophilicity of the ester-type oxygen at C-20 would not give rise to a cyclic oxocarbenium ion, thus allowing for rearrangement of the steroid ring system. Treatment of **1** with an excess of MCPBA in different solvent systems resulted in regioselective migration of the C13–C17 bond (Table 1, entries 1–3). In all cases the expected olefin **2** was epoxidized in the reaction medium, yielding the 13,14-epoxide mixture **3** and **4**. Formation of the epoxides was evident in the ^{13}C NMR spectrum of the mixture where two pairs of resonances for non-protonated

† Electronic supplementary information (ESI) available: AM1 calculated structures for the most stable conformers of the iodosyl derivative of 18-iodopregnane **1**; the C-18 carbocation derived from **1** and the iodosyl derivative of 20*R*-iodopregnane **9a**. See http://www.rsc.org/suppdata/p1/b1/b102688g/

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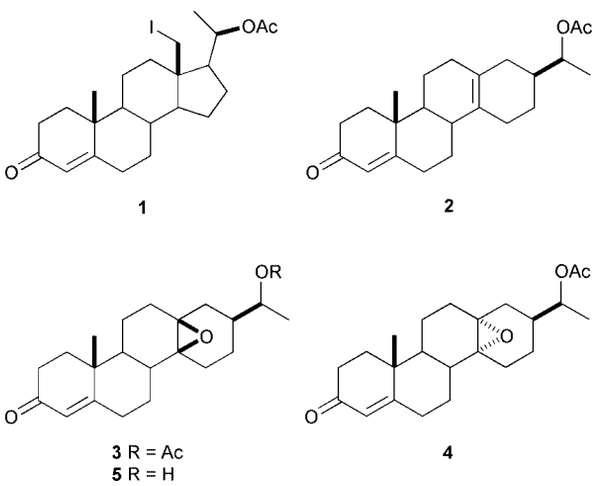
Table 1 Reaction of iodopregnanes with MCPBA

Entry	Substrate	MCPBA (equiv.)	Solvent[a]	Time (*t*/h)	Temp (*θ*/°C)	Product (yield, %)[b]
1	**1**	6	A	3	25	**3** + **4** (1 : 1.5, 77)
2	**1**	6	B	2	0	**3** + **4** (1 : 1.5, 60)
3	**1**	8[c]	C	3	25	**3** + **4** (1 : 3, 81)
4	**9a**	2.8	D	1	0	**10** (50); **11** (45)
5	**9a**	5	A	3	25	**10** (75); **11** (8)
6	**9a**	5	E	3	25	**10** (81)
7	**9a**	8[c]	C	3	25	**12** (80)
8	**9b**	2.8	D	1	0	**11** (22); **14** (23); **13** (54)
9	**9b**	5	A	3	25	**10** (40); **13** (44)
10	**9b**	5	E	3	25	**10** (42); **13** (49)
11	**9b**	8[c]	C	5	25	**12** (11); **15** (49)

[a] A, Bu^{t}OH–THF–water (3 : 2 : 1); B, Bu^{t}OH–Cl_2CH_2–water (3 : 2 : 1); C, dry methanol; D, Cl_2CH_2 saturated with water; E, THF–water (3 : 1). [b] Yields correspond to isolated products. [c] Dry MCPBA was used.



carbons appeared at δ_C 63.8/62.3 and 64.7/63.1, the latter pair being more intense in all cases. Although regioselectivity of bond migration was not dependent on the solvent used, stereoselectivity of the subsequent epoxidation and the overall yield increased when the reaction was carried out in dry methanol (Table 1, entry 3).‡

The structures of epoxides **3** and **4** were established based on the following evidence. Attempts to separate the epoxide mixture by column chromatography were partially successful, yielding only small amounts of the major product **4**. However, upon treatment with 5% NaOH in THF–MeOH products could be separated by flash chromatography on silica gel. The minor component **3** gave the deacetylated derivative **5** which was crystallized and its structure determined to be the 13β,14β-epoxide by X-ray diffraction analysis (Fig. 1a). Reacetylation of **5** gave epoxide **3**, the ^{13}C resonances for carbons 13 and 14 being identical with those observed for the minor constituent in the mixture described above. The major component **4** gave a deacetylated derivative lacking the characteristic epoxide signals observed previously. This compound was assigned structure **6** which would arise from the *in situ* cyclization of the deacetylated epoxide (Scheme 2). This was indicative of the α stereochemistry for epoxide **4**. Diagnostic resonances for ether **6** were the two non-protonated carbons at δ_C 83.8 and 74.6 assigned to C-13 and C-14 respectively; the downfield shifts (compared with **4**) indicated opening of the epoxide. The resonance of H-20 in the ^1H NMR spectrum showed coupling only to the vicinal methyl (H-21); a model of compound **6** had a *ca.* 90° dihedral angle for H-17/H-20, hence no observable coupling is expected between these hydrogens.§

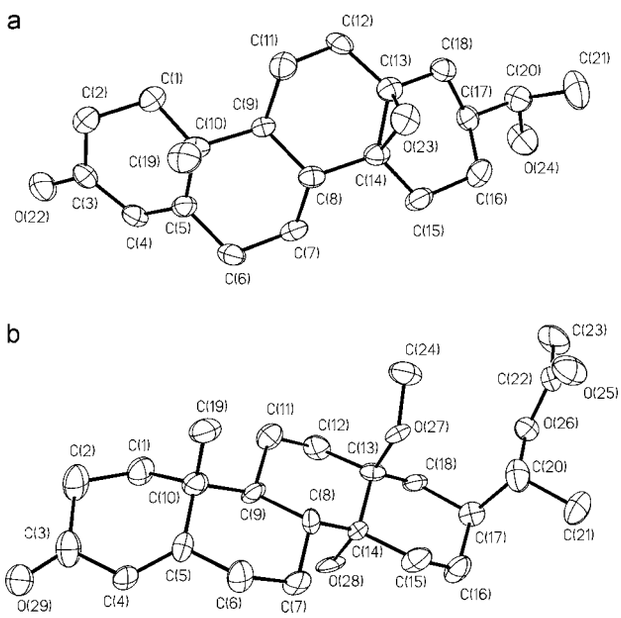
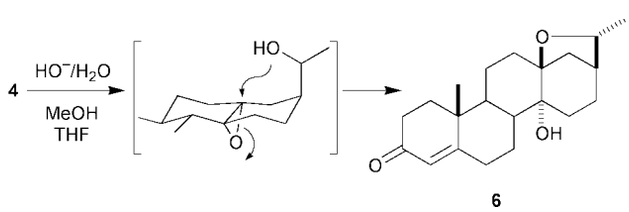


Fig. 1 Displacement ellipsoid diagrams[14] for a) (20*R*)-20-hydroxy-13β,14β-epoxy-17(13→18)-*abeo*-pregn-4-en-3-one **5** and b) (20*R*)-20-acetoxy-14α-hydroxy-13β-methoxy-17(13→18)-*abeo*-pregn-4-en-3-one **7**, showing the numbering scheme used. Displacement ellipsoids drawn at a 40% probability level.



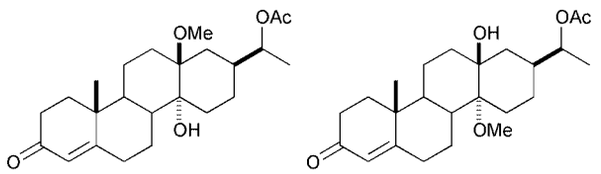
Scheme 2

Confirmation of the structure of **4** came from the methanolysis of the original epoxide mixture. The resulting two methoxy alcohols could be separated and the major product **7**, derived from **4**, gave adequate crystals for X-ray diffraction analysis which showed its structure as the 13β-methoxy-14α-hydroxy derivative (Fig. 1b), the expected product arising from *trans* axial cleavage of the 13α,14α-epoxide. Methanolysis of the minor β-epoxide **3** also resulted in the expected *trans* axial

‡ Reaction of the epimeric (20*S*)-20-acetoxy-18-iodopregn-4-en-3-one with MCPBA under the same conditions showed no differences in the regioselectivity of the rearrangement.

§ The resonance for H-20 in the ^1H NMR spectrum of the C-20 epimeric ether obtained by deacetylation of the epoxide derived from (20*S*)-20-acetoxy-18-iodopregn-4-en-3-one appeared as a double quartet with J = 3.3 and 6.5 Hz.

cleavage product, the 13β-hydroxy-14α-methoxy derivative **8**. This was evident in the 500 MHz NOESY spectrum of **8** which



7 **8**

showed strong correlations of the methoxy group hydrogens (at δ 3.34) with H-7α (δ 1.45), H-16α (δ 1.72) and H-7β (δ 1.98), clearly establishing its position at C-14 with the α stereochemistry.

The above results are in agreement with the occurrence of a regiospecific Wagner–Meerwein-type rearrangement in the iodosyl derivative of 18-iodopregnane **1** with migration of the C13–C17 bond and formation of a 17(13→18)-*abeo*-pregnane. Due to the bulk of the iodoso group its most favourable orientation would be *anti* to the C13–C14 bond, a concerted pathway[5] (sp^3 alignment) would result in migration of that bond with formation of a bicyclo[4.3.1] product. The experimental findings thus are consistent with a non-concerted (sp^2 alignment) pathway *via* a free carbocation on C-18 that may adopt the appropriate alignment for migration of the C13–C17 bond (ring D expansion).¶

The rearrangement of the structurally related 19-iodoandrost-5-enes by peracid oxidation has been reported to give a complex mixture of products of poor synthetic value; however, this was probably due to the homoallylic nature of the iodine substituent in those compounds.[9]

Scope

To expand the scope of this methodology, we carried out MCPBA oxidation on secondary steroidal iodides, namely, the epimeric iodopregnanes **9a** and **9b**. These compounds may be easily prepared from 3-oxo-22,23-dinorchol-4-enoic acid and separated by flash chromatography.[10] The absolute configuration of the major product of the reaction at C-20 was established as 20*S* by X-ray crystallography (Fig. 2). Pregnanes carrying a good leaving group at C-20 easily give Wagner–Meerwein-type rearrangements under a wide variety of conditions.[11] Thus, reaction of **9a** or **9b** with MCPBA under the conditions indicated in Table 1 gave a mixture of substitution and/or rearrangement products depending on the configuration of the iodine-bearing carbon, *i.e.* the 20*R*-iodopregnane **9a** gave only rearrangement products **10**–**12** (Table 1, entries 4–7), while for the 20*S*-iodo epimer substitution products **13**–**15** predominated (Table 1, entries 8–11).

AM1 calculations on the iodosyl derivatives of 20-iodopregnanes **9a** and **9b** showed that the most stable conformer of the 20*R* epimer had its side chain orientated in the ideal antiperiplanar alignment for the observed migration of the C16–C17 bond.‖ The predicted stereochemistry at C-20 for the resulting products **10**–**12** was in agreement with the experimental result, thus supporting a concerted Wagner–Meerwein-type rearrangement (sp^3 alignment) similar to that postulated for the 20β-tosylates.[11a] On the other hand, the possible conformers of the C-20 carbocation resulting from loss of the iodoso group did not show adequate alignment of the C16–C17

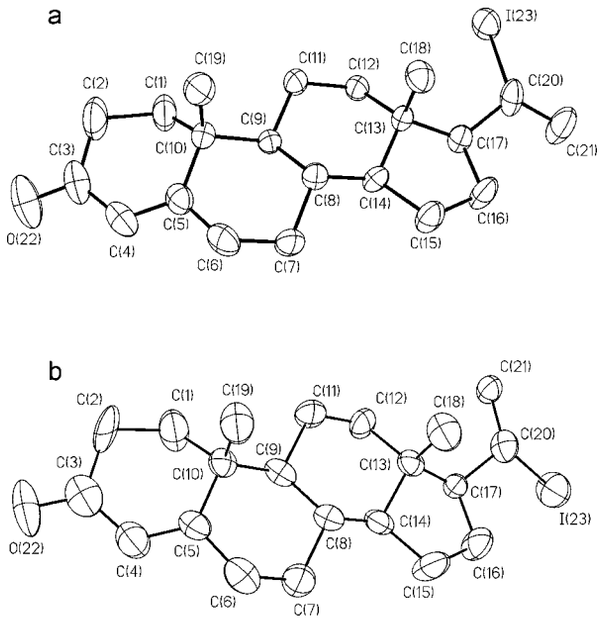
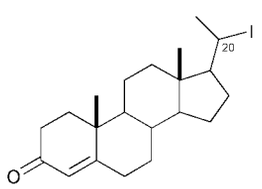
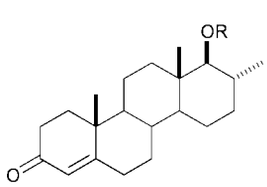


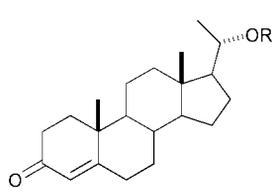
Fig. 2 Displacement ellipsoid diagrams[14] for a) (20*R*)-20-iodopregn-4-en-3-one **9a** and b) (20*S*)-20-iodopregn-4-en-3-one **9b**, showing the numbering scheme used. Displacement ellipsoids drawn at a 40% probability level.



9a 20*R*
9b 20*S*



10 R = H
11 R = 3-ClC_6H_4CO
12 R = Me



13 R = H
14 R = 3-ClC_6H_4CO
15 R = Me

bond for the occurrence of a non-concerted rearrangement. Similar calculations on the iodosyl derivative of the 20*S*-iodopregnane did not favour the antiperiplanar alignment of the C16–C17 bond. The fact that, on the one hand, the substitution products showed retention of configuration at C-20 and, on the other, the rearrangement product was the same as for the 20*R* epimer strongly suggests that the dominant mechanism in this case involves the C-20 carbocation, which is consistent with the more complex mixture of products obtained. The observed rearrangement would thus follow a non-concerted pathway (sp^2 alignment).**

Conclusions

The experimental results presented herein illustrate that iodosyl derivatives may act as masked carbocations and can be used as substrates for Wagner–Meerwein-type rearrangements *via* concerted or non-concerted mechanisms. This methodology is a

¶ See electronic supplementary information at http://www.rsc.org/suppdata/p1/b1/b102688g/

‖ The I–C20–C17–C16 torsion angle of the most stable conformer (171.9°) is very close to the experimental value of −178.3° for the same angle in the 20*R*-iodopregnane **9a** as determined by X-ray crystallography (Fig. 2a).

** It should be noted that nucleophile attack on a steroidal C-20 sp^2 carbon occurs from the less hindered α-face. Furthermore, if the rearrangement were to occur by a concerted pathway the C-17 epimers of compounds **10**–**12** should result.

useful alternative that avoids the drastic acid media and/or heavy metals classically used in these reactions.

Experimental

Mps were taken on a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded in KBr pellets on a Nicolet Magna IR 550 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were measured on a Bruker AC-200 (200.13 and 50.32 MHz) or AM-500 (500.13 and 125.72 MHz) NMR spectrometer for samples in deuteriochloroform (using tetramethylsilane as internal standard). *J*-Values are given in Hertz. Electron-impact mass spectra (EI) were measured in a GC-MS Shimadzu QP-5000 mass spectrometer at 70 eV by direct inlet. Electron-impact high-resolution mass spectra were obtained in a VG ZAB BEQQ mass spectrometer. $[\alpha]_D$-Values are given in 10^{-1} deg cm^2 g^{-1}. Semiempirical calculations were performed with Hyperchem 5.1 (Hypercube Inc.). All solvents used were reagent grade. Solvents were evaporated at $\theta \approx 45$ °C under reduced pressure. Extractive work-up included exhaustive extraction with the solvent indicated, washing successively with brine and water, drying with anhydrous sodium sulfate, and evaporation of the solvent. Flash chromatography was performed on silica gel Merck 9385 (40–63 μ). Reversed-phase column chromatography was performed on octadecyl-functionalized silica gel (Aldrich). Homogeneity of all compounds was confirmed by TLC.

Dry MCPBA was prepared by passing a solution of MCPBA (55% in dry CH_2Cl_2) through anhydrous sodium sulfate (dried at 325 °C for 4 h). The resulting solution was kept for 4 h with anhydrous sodium sulfate and transferred directly to the reaction flask. The solvent was evaporated by passage of a stream of nitrogen and the solid obtained was dried for 1 h at 25 °C and 5×10^{-4} mmHg.

(20*R*)-20-Acetoxy-18-iodopregn-4-en-3-one 1

(20*R*)-20-Acetoxy-18-iodopregn-4-en-3-one **1** was obtained from (20*R*)-20-hydroxypregn-4-en-3-one by conversion to the corresponding 18-iodo derivative with diacetoxyiodobenzene–iodine[10] and acetylation with an excess of acetic anhydride–pyridine (1 : 1). Purification by reversed-phase flash chromatography (MeOH–water, 75 : 25) gave pure acetate **1** as an amorphous solid; ν_{max} (KBr)/cm^{-1} 1730 (C=O, acetate), 1672 (C=C–C=O), 1454, 1372, 1242 (C–O, acetate) and 1083; δ_H (200 MHz) 1.19 (3H, s, 10-H_3C), 1.22 (3H, d, J = 6.1, 20-H_3C), 2.04 (3H, s, acetate), 3.06 (1H, d, J_{gem} = 11.0, 18-H^a), 3.36 (1H, d, J_{gem} = 11.0, 18-H^b), 4.85 (1H, m, 20-H) and 5.74 (1H, br s, 4-H); δ_C (50 MHz) 7.3 (C-18), 17.2 (C-19), 19.2 (C-21), 20.5 (C-11), 22.0 (acetate), 23.8 (C-15), 24.8 (C-16), 31.6 (C-7), 32.5 (C-6), 33.8 (C-2), 35.5 (C-1), 35.9 (C-8), 38.4 (C-10), 39.7 (C-12), 43.4 (C-13), 53.6 (C-9), 55.1 (C-14), 55.3 (C-17), 72.3 (C-20), 124.0 (C-4), 170.0 (C-5), 170.1 (acetate), 199.1 (C-3); *m*/*z* (EI) 357.2422 (M − I. $C_{23}H_{33}O_3$ requires *m*/*z*, 357.2430), 297 (M − I − AcOH, 27), 279 (5), 173 (13), 105 (11) and 43 (100).

Reaction of (20*R*)-20-acetoxy-18-iodopregn-4-en-3-one 1 with MCPBA: (20*R*)-20-acetoxy-13β,14β-epoxy-17(13→18)-*abeo*-pregn-4-en-3-one 3 and (20*R*)-20-acetoxy-13α,14α-epoxy-17(13→18)-*abeo*-pregn-4-en-3-one 4

Method A. To a solution of MCPBA (55%) (1.08 g containing 3.44 mmol) in a mixture of Bu^{t}OH (24 cm^3), THF (2.0 cm^3) and water (8.0 cm^3) was quickly added a solution of **1** (0.28 g, 0.578 mmol) in THF (14 cm^3). The solution was stirred for 3 h at room temperature and 10% aq. $NaHSO_3$ (20 cm^3) was added. The reaction mixture was diluted with ethyl acetate and the organic layer was washed successively with 10% aq. $NaHSO_3$ and brine, dried with Na_2SO_4, and the solvent was evaporated. Fractionation of the residue by flash chromatography (ethyl acetate–hexane, 20 : 80) gave α-*epoxide* **4** (0.045 g, 21%); mp 127–129 °C (from acetone–Pr^{i}OH–hexane) (Found: C, 73.9; H, 8.4. $C_{23}H_{32}O_4$ requires C, 74.2; H, 8.7%); $[\alpha]_D$ +79.2 (*c* 0.53 in $CHCl_3$); λ_{max} (MeOH)/nm 240 (ε/dm^3 mol^{-1} cm^{-1} 12 650); ν_{max} (KBr)/cm^{-1} 1733 (C=O, acetate), 1669 (C=C–C=O), 1455, 1384, 1263 (C–O, acetate), 1042 and 742; δ_H (200 MHz) 1.09 (3H, s, 10-H_3C), 1.16 (3H, d, J = 6.4, 20-H_3C), 2.03 (3H, s, acetate), 4.78 (1H, dq, $J_{20,21}$ = 6.4, $J_{20,17}$ = 4.8, 20-H) and 5.72 (1H, br s, 4-H); δ_C (50 MHz) 16.7 (C-19), 17.3 (C-21), 21.2 (acetate), 21.3 (C-11), 24.6 (C-16), 26.4 (C-15), 27.8 (C-7), 30.1 (C-18), 32.7 (C-6), 33.7 (C-12), 33.9 (C-2), 35.3 (C-8), 35.5 (C-1), 38.0 (C-10), 41.6 (C-17), 45.3 (C-9), 63.1 (C-14), 64.7 (C-13), 73.5 (C-20), 124.3 (C-4), 169.8 (acetate), 170.2 (C-5), 199.5 (C-3); *m*/*z* (EI) 372.2303 (M$^+$. $C_{23}H_{32}O_4$ requires *M*, 372.2301), 330 (M − 42, 3), 312 (M − AcOH, 14%), 294 (M − AcOH − H_2O, 5), 161 (20), 91 (29) and 43 (100).

Continued elution with the same solvent yielded a mixture of *epoxides* **3** and **4** (0.121 g, 56%) in a 1.2 : 1 ratio (^{13}C NMR). Identity of β-epoxide **3** was confirmed by comparison (^{1}H and ^{13}C NMR, TLC) with an authentic sample obtained as described below.

Method B. To a solution of MCPBA (55%) (0.54 g containing 1.72 mmol) in a mixture of Bu^{t}OH (12 cm^3), CH_2Cl_2 (1.0 cm^3) and water (4.0 cm^3) was quickly added a solution of **1** (0.140 g, 0.289 mmol) in CH_2Cl_2 (7.0 cm^3). The solution was stirred for 2 h at 0 °C and 10% aq. $NaHSO_3$ (10 cm^3) was added. Work-up as above and purification by flash chromatography (ethyl acetate–hexane, 20 : 80) gave a mixture of epoxides **3** and **4** (0.065 g, 60%) in a 1 : 1.5 ratio (by ^{13}C NMR).

Method C. To a solution of dry MCPBA [from 1.69 g of MCPBA (55%) containing 5.37 mmol] in dry MeOH (10 cm^3) was quickly added a solution of **1** (0.325 g, 0.671 mmol) in dry MeOH (20 cm^3). The solution was stirred for 3 h at room temperature and 10% aq. $NaHSO_3$ (10 cm^3) was added. After dilution with water, extractive work-up with ethyl acetate as above gave a residue, which was purified by flash chromatography (ethyl acetate–hexane, 20 : 80) to yield a mixture of epoxides **3** and **4** (0.2027 g, 81%) in a 1 : 3 ratio (by ^{13}C NMR).

(20*R*)-20-Hydroxy-13β,14β-epoxy-17(13→18)-*abeo*-pregn-4-en-3-one 5 and (20*R*)-14α-hydroxy-13β,20-epoxy-17(13→18)-*abeo*-pregn-4-en-3-one 6

To a solution of the mixture of epoxides **3** and **4** (1 : 1.5) (0.165 g, 0.443 mmol) in MeOH (12.5 cm^3)–THF (12.5 cm^3) was added 5% aq. NaOH (2.0 cm^3) and the mixture was stirred for 18 h at room temperature under a nitrogen atmosphere. The resulting solution was neutralized with 5% aq. HCl, concentrated *in vacuo*, diluted with water, and extracted with ethyl acetate. The solvent was evaporated and the residue was purified by flash chromatography (ethyl acetate–hexane, 30 : 70) to give *cyclic ether* **6** (0.082 g); mp 178–180 °C (from MeOH) (Found C, 76.0; H, 9.4. $C_{21}H_{30}O_3$ requires C, 76.3; H, 9.2%); $[\alpha]_D$ +82.3 (*c* 0.56 in Cl_3CH); λ_{max} (MeOH)/nm 244 (ε/dm^3 mol^{-1} cm^{-1} 13 650); ν_{max} (KBr)/cm^{-1} 3473 (OH), 1662 (C=C–C=O), 1455, 1284 and 1049 (C–O–C); δ_H (200 MHz) 1.14 (3H, d, J = 6.3, 20-H_3C), 1.17 (3H, s, 10-H_3C), 4.04 (1H, q, J = 6.3, 20-H) and 5.74 (1H, d, J = 1.2, 4-H); δ_C (50 MHz) 18.3 (C-19), 21.7 (C-11), 21.7 (C-15), 21.8 (C-21), 24.8 (C-7), 27.2 (C-16), 31.7 (C-12), 32.4 (C-6), 33.8 (C-2), 35.4 (C-1), 36.6 (C-18), 38.6 (C-10), 40.6 (C-8), 41.7 (C-17), 46.2 (C-9), 74.6 (C-14), 78.2 (C-20), 83.8 (C-13), 123.1 (C-4), 172.1 (C-5), 200.0 (C-3); *m*/*z* (EI) 330.2192 (M$^+$. $C_{21}H_{30}O_3$ requires *M*, 330.2195), 312 (M − H_2O, 14%), 294 (M − 2H_2O, 7), 284 (M − H_2O − CO, 7), 270 (17), 124 (29), 55 (98) and 43 (100).

Continued elution (ethyl acetate–hexane, 40 : 60) gave *20-hydroxy epoxide* **5** (0.051 g); $[\alpha]_D$ +63.6 (*c* 0.51 in $CHCl_3$); λ_{max} (MeOH)/nm 244 (ε/dm^3 mol^{-1} cm^{-1} 11 410); ν_{max} (KBr)/cm^{-1} 3415 (OH), 1669 (C=C–C=O), 1448, 1355 and 875; δ_H (200

MHz) 1.10 (3H, s, 10-H_3C), 1.14 (3H, d, J = 6.3, 20-H_3C), 3.56 (1H, dq, $J_{20,21}$ = 6.3, $J_{17,20}$ = 3.5, 20-H) and 5.73 (1H, br s, 4-H); δ_C (50 MHz) 16.8 (C-19), 18.4 (C-11), 20.5 (C-21), 21.2 (C-18), 28.2 (C-16), 29.6 (C-15), 31.3 (C-7), 33.1 (C-6), 33.6 (C-12), 33.8 (C-2), 35.3 (C-1), 38.9 (C-10), 39.5 (C-8), 40.4 (C-17), 51.2 (C-9), 62.5 (C-14), 64.0 (C-13), 71.5 (C-20), 124.1 (C-4), 169.7 (C-5), 199.2 (C-3); *m*/*z* (EI) 330.2193 (M^+. $C_{21}H_{30}O_3$ requires *M*, 330.2195), 312 (M − H_2O, 2%), 294 (M − 2H_2O, 2%), 279 (8), 149 (29), 55 (92) and 43 (100).

Crystal structure determination of 20-hydroxy epoxide 5

Single crystals of 20-hydroxy epoxide **5** in the form of large plates were obtained from acetone. They were conveniently cut and mounted into glass fibre under a protective coating of inert oil.

Crystal data. $C_{21}H_{30}O_3$, M = 330.45, space group $P2_12_12_1$ (no. 19), a = 7.976(3), b = 9.399(4), c = 4.084(11) Å, V = 1805.5(14) Å^3, Z = 4, D_x = 1.22 g cm^{-3}, $F(000)$ = 720, μ(Mo-Kα) = 0.08 mm^{-1} (no absorption corrections applied), T = 293 K, colourless blocks, 0.28 × 0.22 × 0.18 mm, Siemens R3m diffractometer, $\omega/2\theta$ scans, θ-range: 1.69 to 24.99°. The structure was solved by direct methods[12] and refined by full matrix least squares[13] in F^2 with 1851 independent reflexions to give R_1 = 0.053, wR_2 = 0.090 for 1053 observed reflexions [$I > 2\sigma(I)$] and 249 parameters refined.††

(20*R*)-20-Acetoxy-13β,14β-epoxy-17(13→18)-*abeo*-pregn-4-en-3-one 3

To a solution of 20-hydroxy epoxide **5** (0.025 g, 0.076 mmol) in CH_2Cl_2 (2.0 cm^3) were added acetic anhydride (0.85 cm^3, 9 mmol), triethylamine (1.5 cm^3, 11 mmol) and DMAP (0.003 g, 0.025 mmol). The mixture was stirred for 18 h at 5 °C, diluted with CH_2Cl_2, washed with 5% aq. $NaHCO_3$ and dried with sodium sulfate. Evaporation of the solvent gave *β-epoxide* **3** (0.027 g); mp 112–115 °C (from Pr^i_2O) (Found: C, 74.4; H, 8.9. $C_{23}H_{32}O_4$ requires C, 74.2; H, 8.7%); $[\alpha]_D$ +65.2 (*c* 0.53 in $CHCl_3$); λ_{max} (MeOH)/nm 240 (ε/dm^3 mol^{-1} cm^{-1} 12600); ν_{max} (KBr)/cm^{-1} 1734 (C=O, acetate), 1674 (C=C–C=O), 1452, 1376, 1245 (C–O, acetate), 1045 and 852; δ_H (200 MHz) 1.10 (3H, s, 10-H_3C), 1.14 (3H, d, J = 6.4, 20-H_3C), 2.02 (3H, s, acetate), 4.71 (1H, dq, $J_{20,21}$ = 6.4, $J_{20,17}$ = 4.9, 20-H) and 5.72 (1H, br s, 4-H); δ_C (50 MHz) 16.8 (C-19 and C-21), 18.4 (C-11), 20.8 (C-18), 21.2 (acetate), 28.1 (C-16), 29.6 (C-15), 31.2 (C-7), 33.0 (C-6), 33.5 (C-12), 33.8 (C-2), 35.3 (C-1), 38.0 (C-8), 38.9 (C-10), 39.4 (C-17), 51.1 (C-9), 62.3 (C-14), 63.8 (C-13), 73.6 (C-20), 124.1 (C-4), 169.5 (acetate), 170.6 (C-5), 199.0 (C-3); *m*/*z* (EI) 330 (M − 42, 3%), 312 (M − AcOH, 14), 296 (2), 284 (5), 189 (5), 124 (11), 55 (42) and 43 (100).

(20*R*)-20-Acetoxy-14α-hydroxy-13β-methoxy-17(13→18)-*abeo*-pregn-4-en-3-one 7 and (20*R*)-20-acetoxy-13β-hydroxy-14α-methoxy-17(13→18)-*abeo*-pregn-4-en-3-one 8

To a solution of the mixture of epoxides **3** and **4** (1 : 1.5) (0.175 g, 0.47 mmol) in dry MeOH (40 cm^3) was added 0.5 M methanolic sulfuric acid (1.0 cm^3). The solution was stirred for 1 h at room temperature, neutralized with saturated aq. $NaHCO_3$, and concentrated *in vacuo* to a fifth of its volume. The residue obtained after extractive work-up with ethyl acetate was fractionated by flash chromatography (ethyl acetate–hexane, 20 : 80) to yield *13-methoxy alcohol* **7** (0.082 g); mp 215–217 °C (from acetone) (Found: C, 71.2; H, 9.1. $C_{24}H_{36}O_5$ requires C, 71.3; H, 9.0%); ν_{max} (KBr)/cm^{-1} 3422 (OH), 1727 (C=O, acetate), 1663 (C=C–C=O), 1452, 1251 and 1076; δ_H (200 MHz) 1.20 (3H, s, 10-H_3C), 1.25 (3H, d, J = 6.2, 20-H_3C), 2.03 (3H, s, acetate), 3.05 (3H, s, OCH_3), 5.12 (1H, dq, $J_{20,21}$ = 6.2, $J_{20,17}$ = 9.5, 20-H) and 5.73 (1H, s, 4-H); δ_C (50 MHz) 17.6 (C-19), 19.0 (C-21), 19.3 (C-11), 21.1 (C-16), 21.6 (acetate), 25.3 (C-7), 25.9 (C-15), 32.6 (C-6), 33.9 (C-2), 34.4 (C-12), 35.5 (C-1), 36.9 (C-17), 38.6 (C-18), 38.7 (C-8), 38.9 (C-10), 46.3 (C-9), 47.7 (OMe), 73.2 (C-20), 73.9 (C-14), 76.3 (C-13), 123.3 (C-4), 170.6 (acetate), 171.1 (C-5), 199.5 (C-3); *m*/*z* (EI) 404 (M^+, 27%), 372 (M − MeOH, 6), 354 (M − MeOH − H_2O, 4), 344 (M − AcOH, 5), 326 (M − AcOH − H_2O, 12), 312 (M − AcOH − MeOH, 59), 294 (22), 137 (22), 124 (46), 55 (41) and 43 (100).

Continued elution with the same solvent gave *14-methoxy alcohol* **8** (0.047 g); mp 209–211 °C (from acetone); ν_{max} (KBr)/cm^{-1} 3604 (OH), 1727 (C=O, acetate), 1672 (C=C–C=O), 1456 and 1379; δ_H (500 MHz) 1.16 (3H, s, 10-H_3C), 1.26 (3H, d, J = 6.3, 20-H_3C), 2.09 (3H, s, acetate), 3.34 (3H, s, OCH_3), 5.62 (1H, dq, $J_{20,21}$ = 6.3, $J_{20,17}$ = 9.2, 20-H) and 5.70 (1H, s, 4-H); δ_C (50 MHz) 18.6 (C-19), 19.7 (C-21), 20.4 (C-11), 21.5 (acetate), 22.4 (C-15), 27.4 (C-7), 29.0 (C-16), 33.5 (C-6), 33.7 (C-12), 34.0 (C-2), 34.1 (C-18), 35.6 (C-1), 37.8 (C-8), 38.9 (C-10), 40.1 (C-9), 46.4 (C-17), 52.5 (OMe), 72.0 (C-13), 74.0 (C-20), 78.2 (C-14), 123.1 (C-4), 170.5 (acetate), 171.0 (C-5), 199.8 (C-3); *m*/*z* (EI) 404.2558 (M^+. $C_{24}H_{36}O_5$ requires *M*, 404.2562), 386 (M − H_2O, 1%), 326 (M − H_2O − AcOH, 7.5), 312 (M − AcOH − MeOH, 3), 294 (3), 137 (22), 124 (11), 57 (22) and 43 (100).

Crystal structure determination of 13-methoxy alcohol 7

Single crystals of 13-methoxy alcohol **7** in the form of large plates were obtained from acetone. They were conveniently cut and mounted into glass fibre under a protective coating of inert oil.

Crystal data. $C_{24}H_{36}O_5$, M = 404.53, space group $P2_12_12_1$ (no. 19), a = 7.518(2), b = 16.476(6), c = 17.818(8) Å, V = 2207.2(14) Å^3, Z = 4, D_x = 1.22 g cm^{-3}, $F(000)$ = 880, μ(Mo-Kα) = 0.08 mm^{-1} (no absorption corrections applied), T = 293 K, colourless blocks, 0.32 × 0.20 × 0.17 mm, Siemens R3m diffractometer, $\omega/2\theta$ scans, θ-range: 1.68 to 25.00°. The structure was solved by direct methods[12] and refined by full matrix least squares[13] in F^2 with 2773 independent reflexions to give R_1 = 0.053, wR_2 = 0.090 for 1248 observed reflexions [$I > 2\sigma(I)$] and 302 parameters refined.††

Crystal structure determination of (20*R*)-20-iodopregn-4-en-3-one 9a and (20*S*)-20-iodopregn-4-en-3-one 9b

(20*R*)-20-Iodopregn-4-en-3-one **9a** and (20*S*)-20-iodopregn-4-en-3-one **9b** were obtained as previously described.[10] Crystals of both epimers were obtained by very slow evaporation of a saturated acetone solution. After a few days, quite dissimilar crystals were obtained: while those of compound **9b** grew as very thin plates emerging out of a central nucleus, in a very crowded crystalline conglomerate, those of compound **9a** grew as isolated pinacoidal prisms. In both cases it was necessary to cut the X-ray specimens out of the available material in order to reduce their size to make them suitable for X-ray analysis.

Crystal data of compound 9a. $C_{21}H_{31}IO$, M = 426.36, orthorhombic, space group $P2_12_12_1$ (no. 19), a = 7.887(3), b = 12.510(2), c = 20.083(6) Å, V = 1981.4(9) Å^3, Z = 4, D_x = 1.43 g cm^{-3}, $F(000)$ = 872, μ(Mo-Kα) = 1.620 mm^{-1} (no absorption corrections applied), T = 293 K, crystal dimensions 0.40 × 0.40 × 0.28 mm, Siemens R3m diffractometer, $\omega/2\theta$ scans, θ-range: 1.95 to 25.48°. The structure was solved by direct methods[12] and refined by full matrix least squares[13] in F^2 with 2681 independent reflexions to give R_1 = 0.0319, wR_2 = 0.0785 for 2312 observed reflexions [$I > 2\sigma(I)$] and 211 parameters refined. Flacks parameter (*C*: correct, *I*: inverted chirality) C = −0.01(4), I = 0.99(4); this parameter should be

†† CCDC reference numbers 161559–161562. See http://www.rsc.org/suppdata/p1/b1/b102688g/ for crystallographic files in .cif format.

close to zero for the correct structure and close to one if the chirality is inverted.[15]††

Crystal data of compound 9b. $C_{21}H_{31}IO$, $M = 426.36$, orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 6.696(2)$, $b = 11.819(32)$, $c = 24.686(7)$ Å, $V = 1953.7(10)$ Å^3, $Z = 4$, $D_x = 1.45$ g cm^{-3}, $F(000) = 872$, μ(Mo-Kα) = 1.643 mm^{-1} (no absorption corrections applied), $T = 293$ K, crystal dimensions $0.42 \times 0.38 \times 0.10$ mm, Siemens R3m diffractometer, $\omega/2\theta$ scans, θ-range: 1.65 to 24.97°. The structure was solved by direct methods[12] and refined by full matrix least squares[13] in F^2 with 2071 independent reflexions to give $R_1 = 0.0557$, $wR_2 = 0.1426$ for 1198 observed reflexions [$I > 2\sigma(I)$] and 211 parameters refined. Flacks parameter (*C*: correct, *I*: inverted chirality) $C = -0.02(8)$, $I = 0.90(8)$.[15]††

Reaction of (20*R*)-20-iodo-pregn-4-en-3-one 9a with MCPBA: 17aβ-hydroxy-17α-methyl-D-homoandrost-4-en-3-one 10 and 17aβ-(3-chlorobenzoyloxy)-17α-methyl-D-homoandrost-4-en-3-one 11

Method A. To a solution of dry MCPBA [from 0.411 g of MCPBA (55%) containing 1.31 mmol] in CH_2Cl_2 (20 cm^3)–water (0.125 cm^3) was quickly added a solution of (20*R*)-20-iodopregn-4-en-3-one **9a** (0.200 g, 0.47 mmol) in CH_2Cl_2 (20 cm^3). The resulting solution was stirred for 1 h at 0 °C and 10% aq. $NaHSO_3$ (10 cm^3) was added. The organic layer was washed successively with saturated aq. $NaHCO_3$, brine and water, and dried with Na_2SO_4. Evaporation of the solvent followed by flash chromatography (ethyl acetate–hexane, 10 : 90), gave *chlorobenzoate* **11** (0.096 g, 45%); mp 210–213 °C (from Pr^i_2O) (Found: C, 73.9; H, 7.9. $C_{28}H_{35}ClO_3$ requires C, 73.9; H, 7.8 %); $[\alpha]_D$ +108° (*c* 0.6 in $CHCl_3$); λ_{max} (MeOH)/nm 236 (ε/dm^3 mol^{-1} cm^{-1} 21 700); ν_{max} (KBr)/cm^{-1} 1719 (C=O, benzoate), 1672 (C=C–C=O), 1460, 1287, 1259, 1126, 1078, 969, 742 and 696 (aromatic); δ_H (200 MHz) 0.84 (3H, d, $J_{17,21} = 6.1$, 17-H_3C), 1.04 (3H, s, 10-H_3C), 1.15 (3H, s, 13-H_3C), 4.60 (1H, d, $J_{17a,17} = 10.6$, 17a-Hα), 5.72 (1H, br s, 4-H) and 7.30–8.00 (4H, m, ArH); δ_C (50 MHz) 12.5 (C-18), 17.5 (C-19), 18.6 (C-21), 19.8 (C-11), 23.4 (C-15), 31.3 (C-16), 31.9 (C-17), 32.7 (C-7), 33.1 (C-6), 33.8 (C-2), 35.1 (C-8), 35.4 (C-1), 36.8 (C-12), 38.6 (C-10), 38.8 (C-13), 49.5 (C-14), 53.2 (C-9), 86.8 (C-17a), 123.5 (C-4), 127.7 (C-6′), 129.5 (C-5′), 129.7 (C-2′), 129.8 (C-1′), 132.3 (C-4′), 134.5 (C-3′), 165.2 (Ar*C*O$_2$), 170.5 (C-5), 199.2 (C-3); *m*/*z* (EI) 454.2275 (M$^+$. $C_{28}H_{25}ClO$ requires *M*, 454.2275), 412 (12%), 298 (M − $C_7H_4ClO_2$, 43), 256 (17), 161 (20), 175 (43), 139 (100), 111 (35) and 55 (39).

Continued elution with ethyl acetate–hexane (30 : 70) gave the *D-homoandrostenone* **10** (0.074 g, 50%); mp 178–180 °C (from Pr^i_2O) (Found: C, 79.5; H, 10.5. $C_{21}H_{32}O_2$ requires C, 79.7; H, 10.2%); $[\alpha]_D$ +69.6 (*c* 0.6 in $CHCl_3$); λ_{max} (MeOH)/nm 242 (ε/dm^3 mol^{-1} cm^{-1} 14 700); ν_{max} (KBr)/cm^{-1} 3448 (OH), 1666 (C=C–C=O), 1453, 1284, 1238 and 1056; δ_H (200 MHz) 0.85 (3H, s, 13-H_3C), 0.96 (3H, d, $J_{17,21} = 6.2$, 17-H_3C), 1.16 (3H, s, 10-H_3C), 2.71 (1H, d, $J_{17a,17} = 10.6$, 17a-Hα) and 5.72 (1H, br s, 4-H); δ_C (50 MHz) 11.5 (C-18), 17.6 (C-19), 19.2 (C-21), 20.1 (C-11), 23.5 (C-15), 31.4 (C-16), 32.9 (C-6), 32.9 (C-7), 33.5 (C-17), 33.9 (C-2), 35.2 (C-8), 35.5 (C-1), 37.2 (C-12), 38.8 (C-10), 38.8 (C-13), 49.6 (C-14), 53.4 (C-9), 85.2 (C-17a), 123.4 (C-4), 171.2 (C-5), 199.4 (C-3); *m*/*z* (EI) 316 (M$^+$, 18%), 301 (M − CH_3, 6), 283 (M − CH_3 − H_2O, 43), 274 (6), 175 (20), 69 (100) and 43 (94).

Method B. To a solution of MCPBA (55%) (0.370 g containing 1.18 mmol) in a mixture of Bu′OH (12.0 cm^3), THF (2.0 cm^3) and water (4.0 cm^3) was quickly added a solution of **9a** (0.100 g, 0.234 mmol) in THF (6.0 cm^3). The resulting solution was stirred for 3 h at room temperature and 10% aq. $NaHSO_3$ (10 cm^3) was added. The reaction mixture was diluted with ethyl acetate, washed successively with saturated aq. $NaHCO_3$, brine and water, and dried with Na_2SO_4. Evaporation of the solvent and fractionation by flash chromatography (ethyl acetate–hexane, 10 : 90) yielded chlorobenzoate **11** (0.009 g, 8%). Continued elution with ethyl acetate–hexane (30 : 70) gave the D-homoandrostenone **10** (0.056 g, 75%). Both compounds were identical (NMR, TLC) with those obtained above.

Method C. To a solution of MCPBA (55%) (0.310 g containing 0.99 mmol) in THF (5.0 cm^3)–water (5.0 cm^3) was quickly added a solution of **9a** (0.085 g, 0.199 mmol) in THF (10 cm^3). The resulting solution was stirred for 3 h at room temperature and 10% aq. $NaHSO_3$ (10 cm^3) was added. The reaction mixture was diluted with ethyl acetate and the organic layer was washed successively with saturated aq. $NaHCO_3$, brine and water, and dried with Na_2SO_4. Evaporation of the solvent followed by purification by flash chromatography (ethyl acetate–hexane, 30 : 70) yielded the D-homoandrostenone **10** (0.051 g, 81%) identical (NMR, TLC) with that obtained above.

Reaction of (20*R*)-20-iodopregn-4-en-3-one 9a with MCPBA–MeOH: 17aβ-methoxy-17α-methyl-D-homoandrost-4-en-3-one 12

To a solution of dry MCPBA [from 0.381 g of MCPBA (55%) containing 1.21 mmol] in dry MeOH (5.0 cm^3) was quickly added a solution of **9a** (0.065 g, 0.152 mmol) in dry MeOH (10 cm^3). The solution was stirred for 3 h at room temperature and 10% aq. $NaHSO_3$ (10 cm^3) was added. The reaction mixture was diluted with water and exhaustively extracted with ethyl acetate. Evaporation of the extract followed by purification by flash chromatography (ethyl acetate–hexane, 3 : 97) gave *D-homoandrostenone* **12** (0.040 g, 80%); mp 141–142 °C (from acetone) (Found: C, 79.6; H, 10.6. $C_{22}H_{34}O_2$ requires C, 80.0; H, 10.4%); $[\alpha]_D$ +50.5 (*c* 0.6 in $CHCl_3$); λ_{max} (MeOH)/nm 244 (ε/dm^3 mol^{-1} cm^{-1} 15 500); ν_{max} (KBr)/cm^{-1} 1678 (C=C–C=O), 1453, 1233, 1184 and 1099 (C–O, OMe); δ_H (200 MHz) 0.84 (3H, s, 13-H_3C), 0.96 (3H, d, $J_{17,21} = 6.1$, 17-H_3C), 1.17 (3H, s, 10-H_3C), 2.21 (1H, d, $J_{17a,17} = 10.1$, 17a-Hα), 3.74 (3H, s, OCH_3) and 5.72 (1H, br s, 4-H); δ_C (50 MHz) 11.3 (C-18), 17.5 (C-19), 19.2 (C-21), 19.9 (C-11), 23.4 (C-15), 31.4 (C-16), 32.8 (C-7), 33.6 (C-6), 33.8 (C-17), 33.9 (C-2), 35.1 (C-1), 35.4 (C-8), 37.5 (C-12), 38.7 (C-13), 39.9 (C-10), 49.9 (C-14), 53.5 (C-9), 62.2 (OMe), 96.1 (C-17a), 123.4 (C-4), 171.3 (C-5), 199.4 (C-3); *m*/*z* (EI) 330 (M$^+$, 35%), 315 (M − 15, 4), 298 (M − MeOH, 10), 288 (M − 42, 8), 256 (M − 42 − MeOH, 7), 124 (30), 105 (25), 85 (60) and 55 (100).

Reaction of (20*S*)-20-iodopregn-4-en-3-one 9b with MCPBA

Method A. Reaction of iodopregnane **9b** (0.180 g, 0.42 mmol) with MCPBA as for the epimeric 20-iodopregnane **9a** (method A), and fractionation by flash chromatography (ethyl acetate–hexane, 10 : 90), yielded a mixture of chlorobenzoates **11** and **14** (0.0792 g, 45%) in a 1 : 1.3 ratio (by ^{1}H NMR), the latter identified upon hydrolysis as described below. Continued elution with ethyl acetate–hexane (30 : 70) gave (20*S*)-20-hydroxypregn-4-en-3-one (**13**) (0.072 g, 54%) identical (NMR, TLC) with an authentic sample. To the mixture of chlorobenzoates **11** and **14** obtained above (0.040 g, 0.088 mM) in THF (2.0 cm^3)–MeOH (2.0 cm^3) was added aq. 5% NaOH (0.5 cm^3) and the solution was stirred for 12 h at room temperature, then was neutralized with 5% aq. HCl and exhaustively extracted with ethyl acetate. Fractionation by flash chromatography (ethyl acetate–hexane, 10 : 90) gave D-homoandrostenone **10** (0.012 g) identical (NMR, TLC) with that obtained above. Continued elution (ethyl acetate–hexane, 30 : 70) yielded (20*S*)-20-hydroxypregn-4-en-3-one (**13**) (0.0125 g), identical with an authentic sample.

Method B. Reaction of iodopregnane **9b** (0.071 g, 0.167 mmol) with MCPBA as for the epimeric 20-iodopregnane **9a**

(method B) followed by fractionation by flash chromatography (ethyl acetate–hexane, 20 : 80), gave the D-homoandrostenone (**10**) (0.021 g, 40%). Continued elution with the same solvent, gave (20*S*)-20-hydroxypregn-4-en-3-one (**13**) (0.023 g, 44%). Both compounds were identical (NMR, TLC) with those obtained above.

Method C. Reaction of iodopregnane **9b** (0.071 g, 0.167 mmol) with MCPBA as for the epimeric 20-iodopregnane **9a** (method C), followed by fractionation by flash chromatography (ethyl acetate–hexane, 20 : 80), gave D-homoandrostenone **10** (0.022 g, 42%). Continued elution with ethyl acetate–hexane (30 : 70) gave (20*S*)-20-hydroxypregn-4-en-3-one (**13**) (0.026 g, 49%). Both compounds were identical (NMR, TLC) with those obtained above.

Reaction of (20*S*)-20-iodopregn-4-en-3-one 9b with MCPBA–MeOH

Reaction of 20-iodopregnane **9b** (0.060 g, 0.141 mmol) with MCPBA in dry MeOH as for the epimeric 20-iodopregnane **9a** followed by purification by flash chromatography (ethyl acetate–hexane, 3 : 97), gave D-homoandrostane **12** (0.005 g, 11%), identical (NMR, TLC) with that obtained above. Continued elution with the same solvent gave *(20S)-20-methoxypregn-4-en-3-one* **15** (0.023 g, 49%); mp 157–159 °C (from acetone) (Found: C, 79.9; H, 10.6. $C_{22}H_{34}O_2$ requires C, 80.0; H, 10.4%); $[\alpha]_D$ +93.0 (*c* 0.56 in $CHCl_3$); λ_{max} (MeOH)/nm 244 (ε/dm^3 mol^{-1} cm^{-1} 14 600); ν_{max} (KBr)/cm^{-1} 1676 (C=C–C=O), 1465, 1370, 1193 and 1098 (C–O, OMe); δ_H (200 MHz) 0.70 (3H, s, 13-H_3C), 1.15 (3H, d, J = 6.2, 20-H_3C), 1.19 (3H, s, 10-H_3C), 3.29 (3H, s, OCH_3), 3.20 (1H, dq, $J_{20,21}$ = 6.2, $J_{20,17}$ = 5.6, 20-H) and 5.73 (1H, br s, 4-H); δ_C (50 MHz) 12.4 (C-18), 17.2 (C-19), 18.3 (C-21), 20.7 (C-11), 23.9 (C-15), 25.6 (C-16), 31.9 (C-7), 32.8 (C-6), 33.8 (C-2), 35.2 (C-8), 35.6 (C-1), 38.5 (C-10), 38.6 (C-12), 43.1 (C-13), 53.7 (C-9), 55.6 (C-14), 55.6 (OMe), 56.8 (C-17), 78.9 (C-20), 123.7 (C-4), 171.3 (C-5), 199.4 (C-3); *m/z* (EI) 330 (M^+, 9%), 315 (M − CH_3, 2), 298 (M − MeOH, 4), 288 (3), 256 (3), 124 (33), 105 (25), 91 (14) and 59 (100).

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