Photoinduced Molecular Transformations. Part 132.[1] A Two-Step Intramolecular Transposition of the 17β -Acetyl Group of Pregnan-20-one to C-18 through the Formation of Cyclobutanols by the Reaction of the Excited Carbonyl, followed by a Selective β-Scission of Alkoxyl Radicals generated from them.

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New two-step transformations of a pregnan-20-one into 18-functionalized androstanes and 18a,18b-dihomoandrostanes are described; a type-II reaction of an excited pregnan-20-one protected in the A,B-ring gave the corresponding 20-hydroxy-18,20-cyclopregnane. Selective β-scission of the cyclobutanoxyl radicals generated by irradiation of the nitrite or the hypoiodite gave a 5:4 ratio of the corresponding 18a,18b-dihomo-5α-androstan-18a-one and 18-iodoandrostan-17β-yl acetate in 89% yield or 18a,18b-dihomo-5α-androstane-17,18a-dione 17-oxime in 83% yield. The transformation involves a novel two-step intramolecular transposition of the 17β-acetyl group to C-18, and an oxygen insertion to the C-17–C-20 bond of pregnan-20-one.

Several chemoselective transformations of the functional groups of the 18-iodoandrostan-17-one and 18a,18b-dihomo-5α-pregnan-18a-one, including the synthesis of 3β-hydroxy-18a,18b-dihomoandrost-5-ene-17,18a-dione, are reported.

Studies on the functionalization of the inactive 13β-methyl group of the steroidal skeleton have mostly been focused on oxygenation by intramolecular hydrogen abstraction by alkoxyl radicals,[2,3] since the 18-oxygenated steroids include a number of biologically active molecules, such as aldosterone.[4]

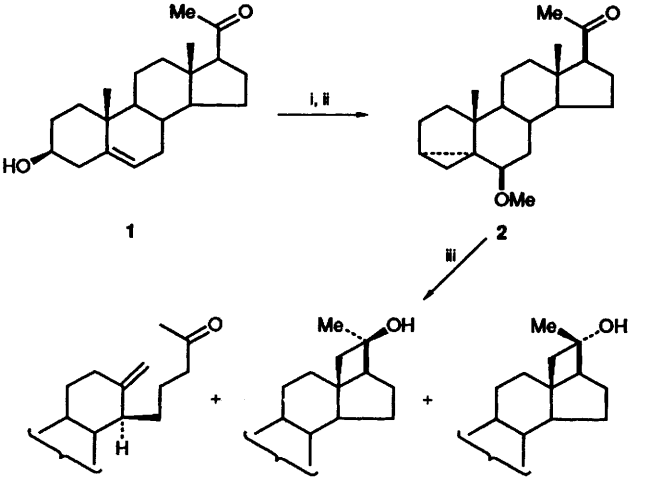
In this paper we report on an acetylation (alkylation) of the 13β-methyl group of steroids by a two-step intramolecular transposition of the 17β-acetyl group of a pregnan-20-one to C-18. The process involves an intramolecular hydrogen abstraction by an excited 20-carbonyl of pregnan-20-one, followed by a selective β-scission of alkoxyl radicals generated from the resulting cyclobutanols. This work was carried out as one part of our programme to explore the synthetic utility of β-scission of alkoxyl radicals[5,6] in general, and cyclobutyloxyl radicals[7] in particular.

Results

It has already been reported by Jeger, Schaffner and collaborators that irradiation of a solution of 5α- and Δ^5-20-oxopregnanes bearing a 3β-acetoxy, 3,3-ethylenedioxy or 11-acetoxy group in ethanol leads to the formation of a mixture of the corresponding stereoisomeric 20-hydroxy-18,20-cyclopregnanes.[8] They ascertained that the major product was the 20β-isomer.[8]

In the present work, 3β-hydroxypregn-5-en-20-one (pregnenolone) **1** was transformed into 6β-methoxy-3α,5-cyclo-5α-pregnan-20-one **2** through the preparation of its tosyl derivative, followed by methanolysis in the presence of sodium acetate according to the standard procedure.[1]

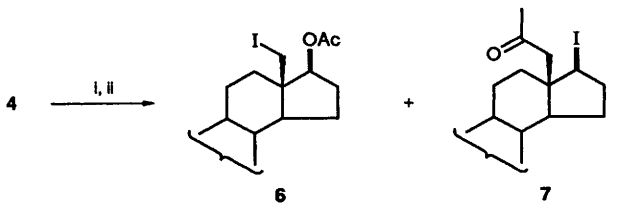
Irradiation of masked pregnane **2** in ethanol in a quartz vessel with UV light gave three products (**3**, **4** and **5**) in 14, 39 and 15% yield, respectively (Scheme 1). The molecular formula of product **3** was confirmed to be $C_{22}H_{34}O_2$ by high-resolution mass spectrometry. The IR spectrum exhibited a band due to an unstrained carbonyl group. The ^{1}H NMR spectrum indicated an absence of the 13β-Me group, and the presence of two doublets at δ 4.62 and 4.74 (each 1 H) assignable to the exomethylene group. The EI mass spectrum exhibited a fragment at *m/z* 275 corresponding to $(M - CH_3COCH_2CH_2CH_2)^+$. These results indicated that product **3** was 6β-methoxy-13-methylene-3α,5-cyclo-18-nor-13,17-seco-5α-pregnan-20-one. This open-chain compound **3** arose by a β-scission of the 1,4-biradical intermediate produced by intramolecular hydrogen abstraction by the excited carbonyl group.



Scheme 1 *Reagents and conditions:* i, *p*-$MeC_6H_4SO_2Cl$–pyridine, room temp.; ii, AcOK–MeOH, reflux; iii, *hν*, EtOH, room temp.

Products **4** and **5** were stereoisomers having the molecular formula $C_{22}H_{34}O_2$. Their IR spectra indicated the absence of a carbonyl group and the presence of a hydroxy group. The ^{1}H NMR spectra exhibited no signal due to an acetyl group. These results immediately indicated that the products are isomeric cyclobutanols (**4** and **5**) arising from bonding of a 1,4-biradical formed by intramolecular hydrogen abstraction by the excited 20-carbonyl; the major product **4** was the 20β-isomer.

We then studied the β-scission of the alkoxyl radical generated from the cyclobutanol **4**. Irradiation of the hypoiodite prepared *in situ* by the reaction of the major cyclobutanol **4** with three molar equivalents of red mercury(II) oxide and iodine in benzene, with Pyrex-filtered light under standard conditions,[1,7] gave two products (**6** and **7**) in 51 and 38% yield, respectively (Scheme 2).



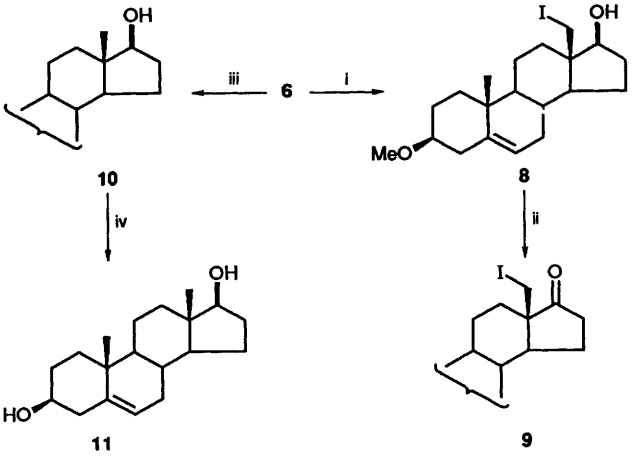
Scheme 2 *Reagents and conditions:* i, $HgO–I_2,C_6H_6$ or $LTA–I_2$, C_6H_6; ii, *hν*

Mass spectrometry and combustion analysis indicated that the crystalline product **6** had the molecular formula $C_{22}H_{33}IO_3$. The IR spectrum exhibited a band ascribable to an unstrained carbonyl group. The ^1H NMR spectrum showed signals attributable to the acetoxy and 6β-methoxy groups. The spectrum also exhibited a methylene proton bearing an iodine as well as a proton attached to a carbon bearing an acetoxy group. These results, together with the probable genesis, indicated that product **6** was 6β-methoxy-18-iodo-3α,5-cyclo-5α-androstan-17β-yl acetate.

High-resolution mass spectrometry indicated that product **7** had the molecular formula of $C_{22}H_{33}IO_2$. The IR spectrum exhibited the presence of an unstrained carbonyl group. The ^1H NMR spectrum showed the absence of 13β-Me and the presence of a triplet at δ 3.73, assignable to a proton attached to the carbon atom bearing an iodine atom. These results, together with a consideration of the probable formation pathway, indicated that product **7** was 17β-iodo-6β-methoxy-3α,5-cyclo-18a,18b-dihomo-5α-androstan-18a-one.*

Irradiation of the hypoiodite prepared *in situ* by reaction of the cyclobutanol **4** with lead tetracetate (LTA) and iodine[2b] in benzene similarly gave two products (**6** and **7**), but in lower yield (26 and 32%).

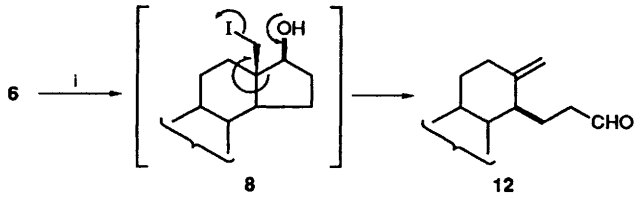
The reduction of 18-iodide **6** with lithium aluminium hydride in diethyl ether at room temperature afforded a product **10**, the spectral data of which were in accord with 6β-methoxy-3α,5-cyclo-5α-androstan-17β-ol (52% yield). Its treatment with toluene-*p*-sulfonic acid (PTSA) gave androst-5-ene-3β,17β-diol **11** in 78% yield. Acidic hydrolysis of the 17-acetate **6** with PTSA in methanol at 80 °C gave 3β-methoxy-18-iodoandrost-5-en-17β-ol **8** in 56% yield by simultaneous regeneration of the 5-ene structure. Oxidation of 17β-ol **8** with pyridinium dichromate (PDC) at room temperature gave the 18-functionalized androstane **9** in 52% yield (Scheme 3).



Scheme 3 *Reagents and conditions:* i, PTSA–MeOH, 80 °C; ii, PDC–CH_2Cl_2, room temp.; iii, $LiAlH_4$–Et_2O, room temp.; iv, PTSA, aq. 1,4-dioxane, 100 °C

* Nomenclature according to 1989 IUPAC recommendations: *Pure Appl. Chem.*, 1989, **61**, 1783.

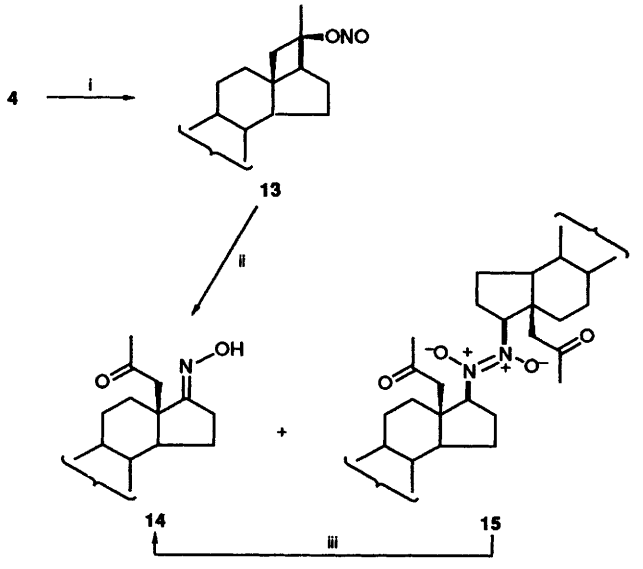
On the other hand, basic hydrolysis of 17-acetate **6** with potassium carbonate in methanol–water resulted in the formation of 13,17-secosteroid **12** in 92% yield, which arose from hydrolysis of the acetoxy group followed by base-catalysed fragmentation (Scheme 4).



Scheme 4 *Reagents and conditions:* i, K_2CO_3 aq. MeOH, room temp.

We then turned our attention to a study of the β-scission of alkoxyl radicals generated from nitrite by UV irradiation.

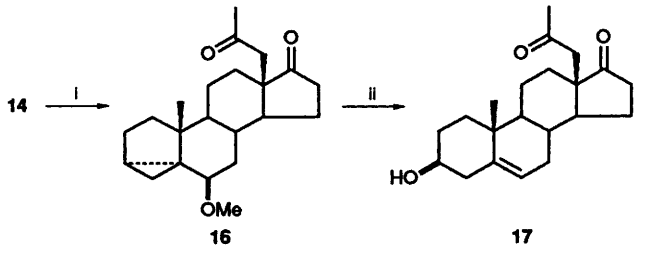
The nitrite **13** of the cyclobutanol **4**, prepared by the standard procedure,[9] was photolysed in benzene with Pyrex-filtered light to give two products (**14** and **15**) in 49 and 34% yield (Scheme 5). High-resolution mass spectrometry indicated that product **14** had the molecular formula $C_{22}H_{33}NO_3$. The IR spectrum indicated the presence of unstrained carbonyl and hydroxyimino groups. The ^1H NMR spectrum exhibited a singlet (3 H) at δ 2.10 assignable to the acetyl group. These results immediately indicated that the product was (*E*)-6β-methoxy-3α,5-cyclo-18a,18b-dihomo-5α-androstane-17,18a-dione 17-oxime **14**, arising from β-scission of the alkoxyl radical generated from nitrite **4**.



Scheme 5 *Reagents and conditions:* i, NOCl–pyridine, room temp.; ii, *hν*; iii, Pr^iOH, 40 °C

The IR spectrum of product **15** showed a band due to the unstrained carbonyl group. ^1H NMR spectrum of product **15** exhibited a 2 H doublet at δ 6.06, in addition to three 6 H singlets at δ 1.00, 2.13 and 3.36. These spectral results suggested that product **15** was a dimer of 6β-methoxy-17β-nitroso-3α,5-cyclo-18a,18b-dihomo-5α-androstan-18a-one. The structure of product **15** was then confirmed by formation of the oxime **14** when dimer **15** was heated in isopropyl alcohol.

Treatment of steroidal oxime **15** with sodium nitrite and glacial acetic acid in water at room temperature[11] gave 6β-methoxy-3α,5-cyclo-18a,18b-dihomo-5α-androstane-17,18a-dione **16** in 71% yield. The functional groups of rings A and B of the masked androstan-17-one **16** were then



Scheme 6 *Reagents and conditions:* i, $NaNO_2$, aq. AcOH, room temp.; ii, PTSA, aq. 1,4-dioxane, 100 °C

regenerated by its treatment with PTSA to give 3β-hydroxy-18a,18b-dihomoandrost-5-en-17,18a-dione **17** (Scheme 6).

Discussion

The foregoing results have shown that a combination of the type-II reaction of the excited carbonyl and a selective β-scission of the alkoxyl radicals generated from the resulting cyclobutanols is useful for functionalizing the nonactivated C-13β atoms of steroids.

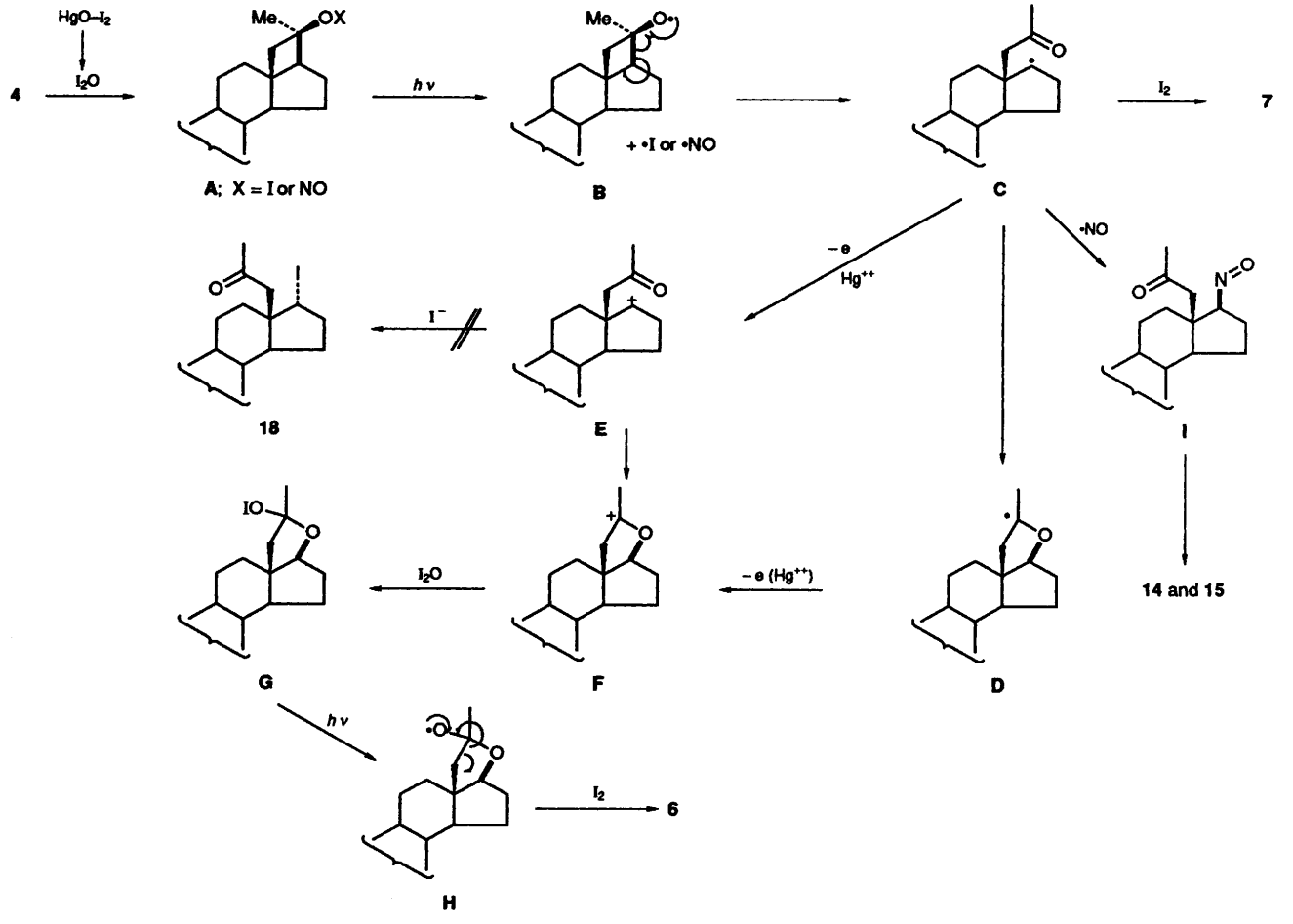
Thus, the foregoing experiments have shown that the 18-iodoandrostane derivative **6** and the 18a-oxo-18a,18b-dihomoandrostane derivative **7** can be obtained in an unconventional manner by photolysis of the hypoiodite of the cyclopregnan-20β-ol **4**, and that the 18a-oxo-18a,18b-dihomoandrostane **14** can be obtained by photolysis of the nitrite **13** of the cyclopregnan-20β-ol **4** in one step.

These novel transformations are believed to be of value since they provide a method for 3- or 4-step transformations of commercially available pregnenolone into 18-functionalized androstanes and 18a-functionalized 18a,18b-dihomoandrostanes, both bearing another functional group at their 17-position.

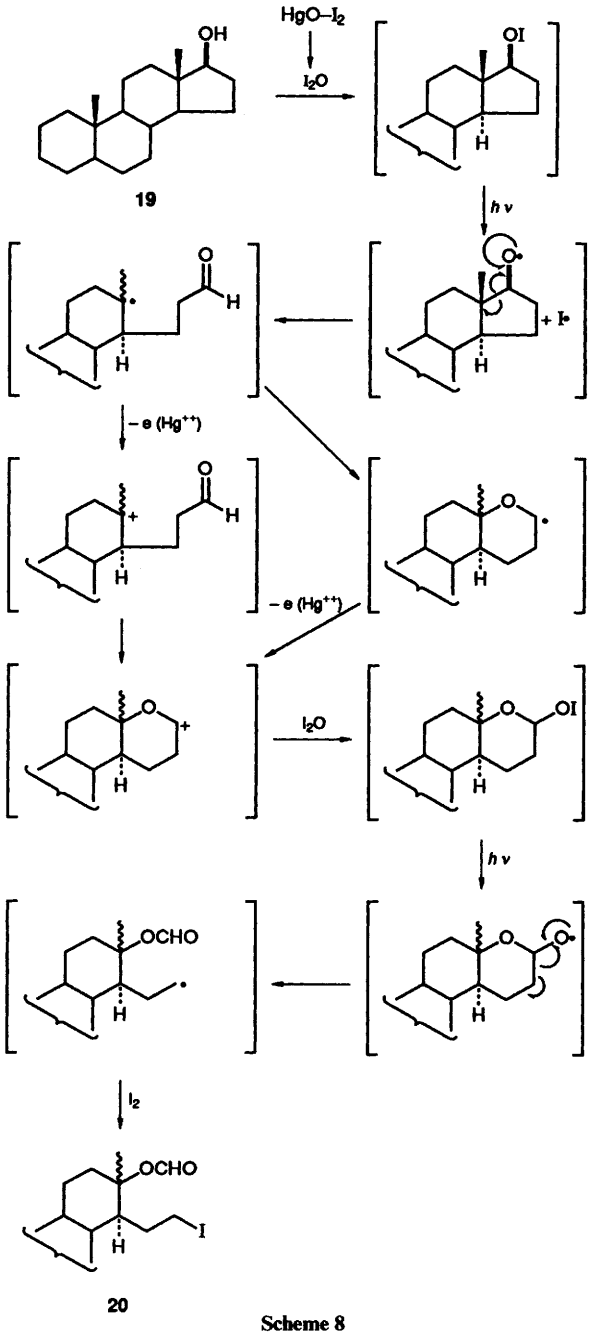
We have, in fact, achieved several chemoselective transformations of the functionalized androstane **6** as well as of the 18a,18b-dihomoandrostane **14**.

The pathways leading to the 18-functionalized steroids **6**, **7**, **14**, and **15** are outlined in Scheme 7; the formation of the 18-iodoandrostane **6** during the irradiation of the hypoiodite of the cyclobutanol **3** is entirely analogous to the formation of an iodo formate (*e.g.*, **20** in Scheme 8) in the photolysis of the hypoiodites of steroidal 17-ols (*e.g.* **19** in Scheme 8) reported previously by us.[12a] We have already shown the underlying mechanism of this novel reaction in terms of Scheme 8 by ^{18}O-labelling studies.[12a,c] Since then, we have found a number of examples of this reaction with a variety of substrates.[7c,12]

On the basis of these results obtained in past studies, the pathway for the formation of the 18-iodoandrostane **6** can be explained as outlined in Scheme 7. A β-scission of the cyclobutoxyl radical **B** generated from the hypoiodite **A** (X = I) of cyclobutanol **3** takes place selectively at the C-17–C-20 bond to give a secondary carbon radical **C**, since scission of the C-18–C-20 bond would give a less stabilized primary radical. The carbon radical **C** then reacts in two ways: these involve an abstraction of an iodine atom to give product **7** and an intramolecular combination of the carbon-centred radical **C** with the carbonyl oxygen to generate species **D**. A one-electron oxidation of species **D** then generates a cationic species **F**. Species **F** can alternatively be formed *via* species **E**. The combination of species **F** with iodine oxide forms a second



Scheme 7



Scheme 8

hypoiodite **G**. Selective β-scission of the carbon–carbon bond of the second alkoxyl radical **H** generated from the hypoiodite **G** affords the 18-iodoandrostane **6**.

In contrast to the photolysis of the hypoiodite of the cyclobutanol **4**, photolysis of the corresponding nitrite **A** (X = NO) simply gave products **14** and **15** *via* **I**, arising from a combination of the carbon radical **C** with nitric oxide. One of the explanations for this difference in the mode of the reaction between the hypoiodite and the nitrite would be as follows: in the photolysis of the hypoiodite, part of the carbon-centred radical **C** may be oxidized through the assistance of metal ions to the carbocation **E**, which then cyclizes to intermediate **F** and finally gives product **6**. This would imply that the second hypoiodite **G** might likely be formed by an ionic cyclization of intermediates **E** through **F**, but not though **D** and **F**. The stereoselective formation of 17β-iodide **7** indicates the intervention of the carbon radical **C**, but not carbocation **E**, as the immediate precursor for the formation of iodide **7**, since the reaction of carbocation **E** with iodide ion should result in the formation of α-iodide **18**.

Experimental

M.p.s were recorded with a Yanagimoto melting-point apparatus, and are uncorrected. IR spectra were determined for Nujol mulls with a Hitachi 285 infrared spectrometer, unless stated otherwise. The ^{1}H NMR spectra were determined either with a JEOL JNM-GX 270 spectrometer (270 MHz) or with a JEOL EX-400 spectrometer (400 MHz). $CDCl_3$ was used as the solvent with $SiMe_4$ as an internal standard. The *J*-values are given in Hz. Preparative TLC (PLC) was carried out with Merck Kieselgel 60-PF_{254}. The high- and low-resolution mass spectra were determined with a JEOL JMS-300 spectrometer (70 eV, Faculty of Pharmaceutical Sciences of this University). Elemental analyses were performed by the staff of the analytical laboratory of the Faculty of Pharmaceutical Sciences.

Photoreaction of 6β-*Methoxy*-3α,5-*cyclo*-5α-*pregnan*-20-*one* **2**.[1]—A solution of cyclosteroid **2** (177 mg, 0.54 mmol), prepared from pregnenolone **1** by the standard method,[1] in ethanol (27 cm^3) was placed in a quartz vessel and irradiated for 3 h with a 100 W high-pressure Hg arc (Eikosha). The colourless oil obtained by removal of the solvent was subjected to PLC [(2:1) hexane–ethyl acetate] to give three fractions (A, B and C). The most mobile fraction (A 24 mg, 14%) was *compound* **3** (Found: M^+, 330.2554. $C_{22}H_{34}O_2$ requires *M*, 330.2559); ν_{max}(neat)/cm^{-1} 1715 (C=O), 1643 (C=C), 1094, 1017 and 888; δ(270 MHz) 0.95 (3 H, s, 19-H_3), 2.14 (3 H, s, 21-H_3), 2.81 (1 H, t, *J* 2.9, 6α-H), 3.32 (3 H, s, OMe), 4.62 and 4.74 (each 1 H, each d, *J* 0.73, 18-H); *m/z* 330 (M^+ 1.7%). 315 [$(M - Me)^+$, 11.6), 298 [$(M - CH_3OH)^+$, 27.6], 283 [$(M - CH_3 - CH_3OH)^+$, 10.0], 275 (30.0), 213 (31.7), 91 (47.7) and 43 (100).

The second mobile fraction (69 mg, 39%) gave *the cyclobutanol* **4**, m.p. 129–130 °C (from acetone) (Found: C, 79.8; H, 10.6. $C_{22}H_{34}O_2$ requires C, 79.95; H, 10.37%); ν_{max}/cm^{-1} 3292 (OH), 1196, 1096 and 1078; δ(270 MHz) 0.96 (3 H, s, 19-H_3), 1.11 (3 H, s, 21-H_3) and 3.33 (3 H, s, OMe); *m/z* 330 (M^+, 43.8%), 240 {[M – MeOH – $(CH_3)_2CO$]$^+$, 92.7}, 217 (100), 191 (85.8), 119 (91.3) and 43 (74.7).

The most polar fraction (27 mg, 15%) was the *isomeric cyclobutanol* **5**, m.p. 155–156 °C (from MeOH) (Found: C, 79.8; H, 10.25); ν_{max}/cm^{-1} 3458 (OH), 1227 and 1085; δ(270 MHz) 0.95 (3 H, s, 19-H_3), 1.37 (3 H, s, 21-H_3), 2.78 (1 H, t, *J* 2.93, 6α-H) and 3.33 (3 H, s, OMe); *m/z* 330 (M^+, 3.53%), 315 [$(M - Me)^+$, 10.9], 298 [$(M - MeOH)^+$, 25.5], 283 [$(M - CH_3OH - Me)^+$, 9.9], 272 {[M – $(Me)_2CO$]$^+$, 30.0}, 257 (29.3), 240 (62.0), 217 (63.1), 119 (79.5), 91 (78.1), 79 (70.2) and 43 (100).

β-*Scission Reaction of Alkoxyl Radical Generated by Irradiation of the Hypoiodite of* 6β-*Methoxy*-3α,5α;18,20-*dicyclopregnan*-20β-*ol* **4**.—(a) *With mercury*(II) *oxide and iodine*. To a solution of cyclosteroid **4** (229 mg, 0.69 mmol) in benzene (35 cm^3) in a Pyrex vessel were added red mercury(II) oxide (301 mg, 1.39 mmol) and iodine (367 mg, 1.44 mmol). The solution was then flushed with nitrogen and irradiated with a 100 W high-pressure Hg arc for 3 h while being stirred and cooled with water. The solution was then filtered through Celite, and the filtrate was washed successively with 5% aq. sodium thiosulfate, water and brine, and dried over anhydrous sodium sulfate. After removal of the solvent, the oily residue was subjected to PLC [(5:1) hexane–ethyl acetate] to give two products, **6** and **7**.

The more mobile product **6** (168 mg, 51%) was 18-*iodo*-6β-*methoxy*-3α,5α-*cyclo*-5α-*androstan*-17-*yl acetate*, m.p. 140–141 °C (from MeOH) (Found: C, 55.8; H, 7.1; I, 27.2.

$C_{22}H_{33}IO_3$ requires C, 55.93; H, 7.04; I, 26.86%); ν_{max}/cm^{-1} 1736 (C=O), 1240, 1096 and 1047; δ(270 MHz) 1.03 (3 H, s, 19-H_3), 2.10 (3 H, s, OAc), 2.79 (1 H, t, *J* 3.3, 6α-H), 3.33 (3 H, s, OMe), 3.30 (1 H, d, *J* 10.7, 18-H), 3.40 (1 H, d, *J* 10.7, 18-H) and 4.87 (1 H, t, *J* 8.4, 17α-H); *m/z* 472 (M^+, 3.9%), 457 [$(M - Me)^+$, 8.9], 440 [$(M - MeOH)^+$, 7.9], 417 (16.8), 345 [$(M - I)^+$, 7.0], 253 (24.0), 105 (22.7), 91 (29.5), 79 (26.9) and 43 (100).

The less mobile product **7** (120 mg, 38%) was 18-*acetyl*-17β-*iodo*-6β-*methoxy*-3α,5-*cyclo*-5α-*androstane* as a glass (Found: M^+, 456.1550. $C_{22}H_{33}IO_2$ requires *M*, 456.1525); ν_{max}(neat)/cm^{-1} 1708 (C=O), 1094, 1016 and 755; δ(270 MHz) 1.01 (3 H, s, 19-H_3), 2.29 (3 H, s, 21-H_3), 2.79 (1 H, t, *J* 2.9, 6α-H), 3.34 (3 H, s, OMe) and 3.73 (1 H, t, *J* 9.8, 17α-H); *m/z* 456 (M^+, 2.38%), 441 [$(M - Me)^+$, 6.16], 424 [$(M - MeOH)^+$, 4.9], 401 (12.1), 329 [$(M - I)^+$, 67.6], 239 (47.9), 105 (30.0), 91 (43.2), 79 (38.2) and 43 (100).

(b) *With lead tetraacetate–iodine.* To a solution of cyclosteroid **4** (106 mg, 0.321 mmol) in benzene (16 cm^3) were added LTA (323 mg, 0.656 mmol) and iodine (165 mg, 0.650 mmol). The solution was then irradiated for 3 h while being cooled by water and stirred. The solution was then washed with 5% aq. sodium thiosulfate. After removal of a yellow solid by filtration, the filtrate was washed successively with 5% aq. sodium sulfate and water, and then dried over anhydrous sodium thiosulfate. Evaporation of the solvent gave a mixture of products, which was subjected to PLC [(3:1) hexane–ethyl acetate] to give three fractions. The most mobile fraction (39 mg, 26%) was the 18-iodoandrostan-17β-yl acetate **6**. The second mobile fraction (47 mg, 43%) was the 18a,18b-dihomoandrostane **7**. The most polar fraction was an intractable mixture.

6β-*Methoxy*-3α,5-*cyclo*-5α-*androstan*-17β-*ol* **10** *by Reduction of the* 18-*Iodide* **6** *with Lithium Aluminium Hydride.*—A solution of 18-iodo steroid **6** (168 mg, 0.356 mmol) in diethyl ether (13 cm^3) containing lithium aluminium hydride (30 mg, 0.79 mmol) was stirred for 2.75 h at room temperature. To this solution was added an additional amount (27 mg) of lithium aluminium hydride in diethyl ether (5 cm^3); the mixture was then stirred for 30 min. Excess of reducing reagent was decomposed by slow addition of water; the solution was then filtered through Celite. The organic layer of the filtrate was washed successively with water and brine, and dried over anhydrous sodium sulfate. Removal of the solvent gave an oily residue, which was subjected to PLC [(3:1) hexane–ethyl acetate] to give the *masked androstane* **10** (56 mg, 52%), m.p. 144–145 °C (from hexane–dichloromethane) (Found; C, 78.7; H, 10.5. $C_{20}H_{32}O_2$ requires C, 78.90; H, 10.59%); ν_{max}/cm^{-1} 3286 (OH), 1095, 912 and 733; δ(400 MHz) 0.80 (3 H, s, 18-H_3), 1.04 (3 H, s, 19-H_3), 2.77 (1 H, t, *J* 2.93, 6α-H), 3.33 (3 H, s, OMe) and 3.65 (1 H, t, *J* 8.79, 17α-H); *m/z* 304 (M^+, 28.7%), 289 [$(M^+ - Me)$, 52.5], 272 [$(M - MeOH)^+$, 55.3], 257 [$(M - Me - MeOH)^+$, 11.8] and 249 (100).

18-*Iodo*-3β-*methoxyandrost*-5-*en*-17β-*ol* **8** *by Hydrolysis of the* 18-*Iodide* **6** *with Toluene*-p-*sulfonic Acid.*—A solution of the 18-iodide **6** (98 mg, 0.208 mmol) and PTSA (33 mg) in methanol (6 cm^3) was heated under reflux for 5.5 h. The solvent was then evaporated off under reduced pressure to give a residue. After addition of water to this residue, the product was extracted with dichloromethane three times. The combined organic layer was washed successively with 5% aq. sodium hydrogen carbonate and water, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave an oily product **8**, which was purified by PLC [(1:1) hexane–ethyl acetate] to give 18-*iodo*-3β-*methoxyandrost*-5-*en*-17β-*ol* **8**, m.p. 135–138 °C (from MeOH) (50 mg, 56%) (Found: M^+, 430.1355. $C_{20}H_{31}IO_2$ requires *M*, 430.1369); ν_{max}/cm^{-1} 3364 (OH), 1097, 1045 and 729; δ(400 MHz) 1.01 (3 H, s, 19-H_3), 3.06 (1 H, m, 3α-H), 3.36 (3 H, s, OMe), 3.23 (1 H, d, *J* 10.7, 18-H), 3.32 (1 H, d, *J* 10.7, 18-H), 3.91 (1 H, t, *J* 8.79, 17α-H) and 5.34 (1 H, d, *J* 5.37, 6-H); *m/z* 430 (M^+, 6.34%), 398 [$(M - MeOH)^+$, 4.26], 303 [$(M - I)^+$, 10.6], 271 [$(M - I - MeOH)^+$, 100], 253 [$(M - I - MeOH - H_2O)^+$, 61.3], 133 (54.5) and 81 (39.9).

18-*Iodo*-3β-*methoxyandrost*-5-*en*-17-*one* **9** *by Oxidation of the* 17β-*ol* **8** *with Pyridinium Dichromate.*—To a solution of the 17β-ol **8** (50 mg, 0.116 mmol) in dichloromethane (6 cm^3) was added a solution of PDC (110 mg, 0.292 mmol) in dichloromethane (4 cm^3). The solution was stirred for 6 h at room temperature and then filtered, and the filtrate was washed twice with water and dried over anhydrous sodium sulfate. Evaporation of the solvent gave an oily product **9**, which was purified by PLC [(3:1) hexane–diethyl ether] to give *crystals*, m.p. 147–149 °C (from MeOH) (26 mg, 52%) (Found: M^+, 428.1194. $C_{20}H_{29}IO_2$ requires *M*, 428.1212); ν_{max}/cm^{-1} 1731 (C=O) and 1096; δ(400 MHz) 1.03 (3 H, s, 19-H_3), 3.07 (1 H, m, 3α-H), 3.36 (3 H, s, OMe), 3.23 (1 H, d, *J* 10.7, 18-H), 3.32 (1 H, d, *J* 10.7, 18-H) and 5.38 (1 H, d, *J* 5.37, 6-H); *m/z* 428 (M^+, 1.10%), 396 [$(M - MeOH)^+$, 0.39], 381 [$(M - MeOH - Me)^+$, 0.52], 301 [$(M - I)^+$, 4.3], 269 [$(M - I - MeOH)^+$, 100], 133 (42.7) and 81 (36.3).

Androst-5-*ene*-3β,17β-*diol* **11**.—To a solution of the steroidal 17β-ol **10** (145 mg, 0.477 mmol) in 1,4-dioxane (10 cm^3) was added a solution of PTSA (33 mg) in water (5.4 cm^3). The solution was heated under reflux for 2 h and poured into ice–water (10 cm^3). The reaction mixture was extracted with diethyl ether three times. The combined organic layer was worked up in the usual way. The product was purified by PLC [(3:1) hexane–ethyl acetate] to give diol **11** (105 mg, 78%), m.p. 172–173 °C (from hexane–dichloromethane) (lit.,[13] 184 °C); δ(270 MHz) 0.82 (3 H, s, 18-H_3), 1.02 (3 H, s, 19-H_3), 3.52 (1 H, m, 3α-H), 3.80 (1 H, t, *J* 8.79, 17α-H) and 5.34 (1 H, d, *J* 5.37, 6-H).

Hydrolysis of 18-*Iodide* **6** *with Potassium Carbonate in Methanol.*—A solution of iodide **6** (46 mg, 0.098 mmol) in methanol (8 cm^3) containing potassium carbonate (34 mg, 0.25 mmol) and water (3 cm^3) was stirred for 1 day at room temperature. The solvent was then removed, and water was added to the residue. The reaction mixture was extracted with diethyl ether three times. The combined extact was washed successively with water containing a small amount of hydrochloric acid, water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave crude secosteroid **12**, which was purified by PLC [(3:1) hexane–ethyl acetate] to give *pure material* **12** (28 mg, 92%) (Found: M^+, 302.2256. $C_{20}H_{30}O_2$ requires *M*, 302.2246); ν_{max}(neat)/cm^{-1} 1721 (CHO), 1084, 912 and 732; δ(400 MHz) 0.96 (3 H, s, 19-H_3) 2.82 (1 H, t, *J* 3.41, 6α-H), 3.32 (3 H, s, OMe), 4.53 (1 H, *J* 1.46, 18-H) and 4.76 (1 H, *J* 1.46, 18-H); *m/z* 302 (M^+, 11.6%), 287 [$(M - Me)^+$, 43.9), 270 [$(M - MeOH)^+$, 33.6], 247 (100), 191 (57.5), 149 (52.2), 105 (52.7), 91 (60.3) and 41 (50.5).

Preparation and Photoreaction of Nitrite **13** *of* 6β-*Methoxy*-3α,5;18,20-*dicyclo*-5α-*pregnan*-20β-*ol* **4** *in Benzene.*—To a solution of the 20β-ol **4** (170 mg, 0.515 mmol) in pyridine (3 cm^3) was added a solution of nitrosyl chloride in pyridine (2 cm^3) prepared by the standard method,[10] at room temperature. The solution was stirred for 5 min and poured into ice–water. Crystals were collected by filtration and dissolved in diethyl ether. The ethereal solution was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave nitrite **13**, which was dissolved in a mixed solvent of benzene (21 cm^3) and methanol (7 cm^3). The solution was irradiated with Pyrex-filtered light for 1 h in an atmosphere of nitrogen while being cooled by an ice-bath. After removal of the solvent with a

rotary evaporator, the yellow oily residue was subjected to PLC [(1:1) benzene–diethyl ether] to give two fractions. The more mobile fraction (91 mg, 49%) was (E)-6β-*methoxy*-3α,5-*cyclo*-18a,18b-*dihomo*-5α-*androstane*-17,18a-*dione* 17-*oxime* **14** as an amorphous compound (Found: M^+, 359.2438. $C_{22}H_{33}NO_3$ requires *M*, 359.2460); ν_{max}/cm^{-1} 3320 (=NOH), 1704 (C=O), 1097, 859, 813 and 735; δ(270 MHz) 1.06 (3 H, s, 19-H_3), 2.10 (3 H, s, Ac), 2.81 (1 H, t, *J* 2.93, 6α-H) and 3.35 (3 H, s, OMe); *m*/*z* 359 (M^+, 5.1%), 344 [$(M - Me)^+$, 18.9], 327 [$(M - MeOH)^+$, 32.9], 302 [$M - CH_3COCH_3$, 55.6), 269 (22.3), 252 (24.5), 105 (40.2), 91 (50.1), 79 (42.5), 105 (40.2), 91 (50.1), 79 (42.6) and 43 (100).

The less mobile amorphous compound (62 mg, 34%) was a *nitroso dimer* **15** (Found: $[(M - C_{22}H_{33}NO_3)^+$, 359.2479. $C_{22}H_{33}NO_3$ requires *M*, 359.2460]; ν_{max}/cm^{-1} 1710 (2 × COMe), 1092 and 753; δ(270 MHz) 1.00 (6 H, s, 19- and 19′H), 2.13 (6 H, s, 2 COMe) and 2.79 (2 H, t, *J* 2.93, 6′α- and 6α-H), 3.36 (6-H, s, 2 × OMe), 6.06 (2 H, d, *J* 6.84, 17α- and 17′α-H); *m*/*z* 359 [$(M - C_{22}H_{33}NO_3)^+$, 2.4%], 344 (8.6), 342 (8.6), 329 (21.1), 302 (26.8), 239 (100), 105 (35.8), 91 (41.8) and 79 (36.2).

Transformation of Nitroso Dimer **15** *into Oxime* **14**.—A solution of the nitroso dimer **15** (3 mg, 0.0042 mmol) in isopropyl alcohol (1.2 cm^3) was warmed for 10 min. Removal of the solvent with a rotary evaporator gave oxime **14** (2 mg, 67%). After purification by PLC, the oxime was identical with the oxime **14** obtained by the aforementioned photoreaction.

6β-*Methoxy*-3α,5-*cyclo*-18a,18b-*dihomo*-5α-*androstane*-17,18a-*diol* **16**.—To a solution of oxime **14** (28 mg, 0.078 mmol) in tetrahydrofuran (1.5 cm^3) were added a sodium nitrite (90 mg, 1.30 mmol) and glacial acetic acid (0.05 cm^3) in water (0.5 cm^3). The solution was stirred for 1 day at room temperature. The solution was then poured into ice–water (3 cm^3). The aqueous mixture was extracted with diethyl ether three times. The ethereal solution was worked up in the usual way. The yellow oily product was subjected to PLC [(1:1) benzene–diethyl ether] to give the 18a,18b-*dihomo*-5α-*androstane*-17,18a-*dione* **16** (19 mg, 71%) as an amorphous solid (Found: M^+, 344.2340. $C_{22}H_{32}O_3$ requires *M*, 344.2351); ν_{max}/cm^1 1740 (5-membered C=O), and 1708 (acetyl); δ(400 MHz) 1.08 (3 H, s, 19-H_3), 2.11 (3 H, s, COMe), 2.84 (1 H, t, *J* 2.93, 6α-H) and 3.36 (3 H, s, OMe); *m*/*z* 344 (M^+, 23.0%), 329 [$(M - Me)^+$, 51.1], 312 [$(M - MeOH)^+$, 53.8], 289 (90.6), 254 (29.8), 105 (46.8), 91 (53.4), 79 (45.0) and 43 (100).

3β-*Hydroxy*-18a,18b-*dihomoandrost*-5-*en*-17,18a-*dione* **17**.—To a solution of the masked 18a,18b-dihomoandrostane **16** (17 mg, 0.049 mmol) in 1,4-dioxane (1.5 cm^3) was added a solution of PTSA (3 mg, 0.016 mmol) and water (0.5 cm^3). The solution was heated under reflux for 1 h. After the addition of more water to the solution, the mixture was extracted with diethyl ether three times. The combined extract was worked up in the usual way. The product was subjected to PLC [(2:1) hexane–ethyl acetate] to give dione **17** as an amorphous solid (Found: M^+, 330.2166. $C_{21}H_{30}O_3$ requires *M*, 330.2181); ν_{max}/cm^{-1} 3332 (OH), 1740 (5-membered C=O), 1708 (C=O), 1096, 1016 and 919; δ(400 MHz) 1.08 (3 H, s, 19-H_3), 2.11 (3 H, s, COMe), 3.50 (1 H, m, 3α-H) and 5.47 (1 H, d, *J* 5.37, 6-H); *m*/*z* 330 (M^+, 7.4%), 315 [$(M - Me)^+$, 73.0], 296 (15.9), 256 (22.2), 145 (42.4), 105 (42.9), 91 (62.3) and 43 (100).

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