Photoinduced Molecular Transformations. Part 131.[1] Synthesis of 18-Norsteroids, Deoxofukujusonorone and the Related Steroids, based on a Selective β-Scission of Alkoxyl Radicals as the Key Step

Hiroshi Suginome,* Yutaka Nakayama and Hisanori Senboku
Organic Synthesis Division, Faculty of Engineering, Hokkaido University, Sapporo 060, Japan

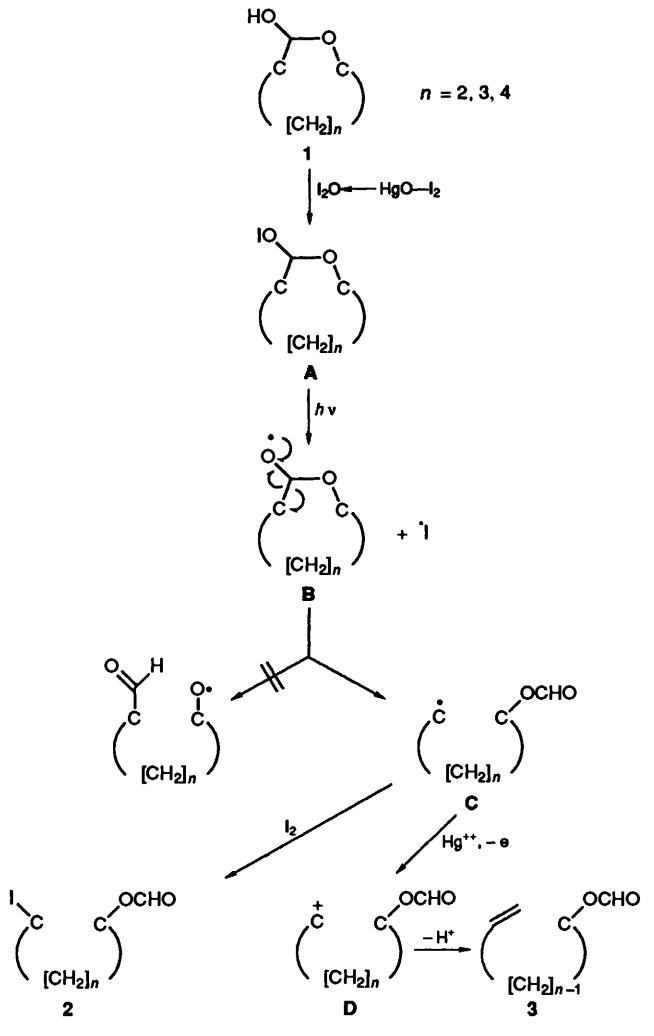
A new transformation of steroids into 18-norsteroids under mild conditions is described. The key step was a regioselective β-scission of the alkoxyl radicals generated by photolysis of the hypoiodite of 18-hydroxy-18,20α-epoxy steroids, prepared by photolysis of steroidal 20α-ol nitrites followed by deoximation of the resulting 18-hydroxyimino-20α-hydroxy steroid with sodium nitrite and acetic acid. 3β-Hydroxypregn-5-en-20-one (pregnenolone) was thus transformed into 3β-hydroxy-18-norpregna-5,13-dien-20-one (12-deoxofukujusonorone) in 10 steps.

Our exploratory studies have indicated that fragmentation of alkoxyl radicals generated from the appropriate hypoiodites by irradiation takes place in a highly selective manner, and is of value in organic transformations. We have demonstrated the utility of selective radical fragmentation in organic synthesis by synthesizing a variety of molecules, including natural products.[2–8]

A new process involving a selective scission of the carbon–carbon bond β to the alkoxyl radicals **B** generated from hypoiodites **A** of lactols **1** (outlined in general Scheme 1) was one of the most useful processes in these syntheses.

A successful application of this process (**1** ⟶ **A** ⟶ **B** ⟶ **C** ⟶ **2** or **D** ⟶ **3**) to the syntheses includes transformations of steroidal cyclic alcohols and ketones into aza-, oxa-, thia-, selena- and tellura-steroids;[2] a new synthesis of lignans;[3] a new general synthesis of medium-ring lactones,[4] macrolides,[5] phthalides and naphthalide lignans;[6] and the transformation of steroids into 19-norsteroids, such as estrone,[7] as well as other products.[8] In this paper, we report on a further application of this process to the transformation of steroids into 18-norsteroids.

Compared with the synthesis of 19-norsteroids,[9] few methods for the synthesis of 18-norsteroids have been reported. These methods include a total synthesis,[10] decarboxylation of 18-oxygenated steroids prepared by hypoiodite reaction,[11] and cleavage and regeneration of the D-ring[12] under rather strong conditions. We have chosen fukujusonorone **4**,[13] the first 18-norsteroid isolated from *Adonis amurensis* Regel et Radd, as the target molecule in the present study, and have achieved a transformation of commercially available 3β-hydroxypregn-5-en-20-one (pregnenolone) **5** into 12-deoxofukujusonorone **22** in 10 steps, as described below.

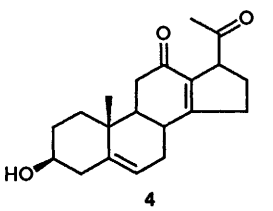


Scheme 1

Results

The functional groups of the A- and B-ring of 3β-hydroxypregn-5-en-20-one **5** (pregnenolone), the starting steroid selected for the transformation into fukujusonorone **4**, were protected by the standard method.[14] Hence, the conversion of pregnenolone **5** into its tosylester, followed by treatment with methanol containing potassium acetate under reflux, gave 6β-methoxy-3α,5-cyclo-5α-pregnan-20-one **6**.[15]

Reduction of the carbonyl group of the masked pregnenolone **6** with sodium and ethanol[16] gave the corresponding 20α-ol **7**[15] as the major product (58%) with accompanying formation of the 20β-isomer **8**[15] (29%), while reduction of 20-ketone **6** with sodium borohydride in ethanol gave the 20β-ol **8** as the major product (79%) as well as the 20α-isomer **7** (13%), as outlined in



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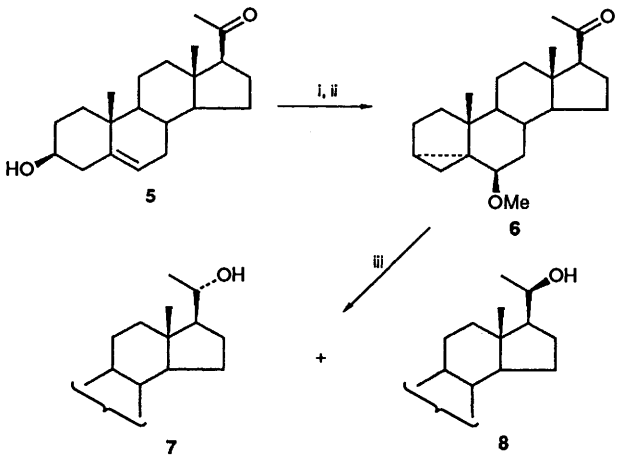
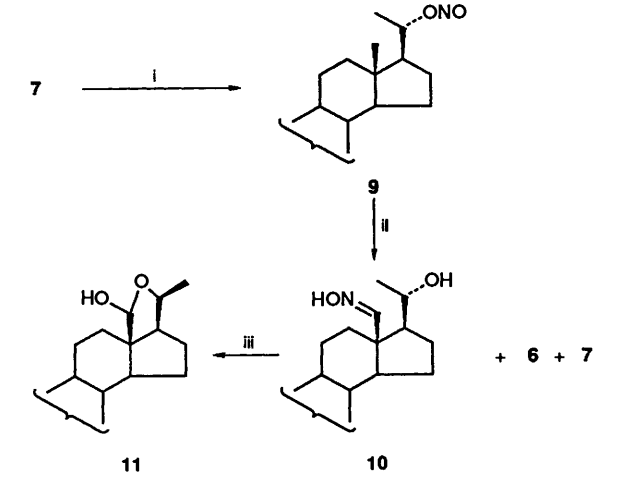


Scheme 2 *Reagents and conditions:* i, TsCl–pyridine; ii, MeOH–AcOK, reflux; iii, Na–EtOH, reflux

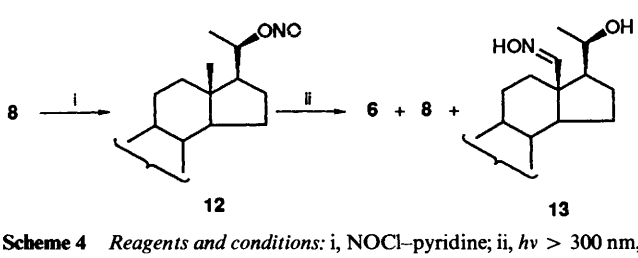
Scheme 2. The predominant formation of the 20β-isomer over its 20α-epimer in the reduction of the steroidal 20-ketone with the complex hydride has been well documented.[17,18]

The 20α-ol **7** was transformed into the corresponding nitrite **9** with nitrosyl chloride in pyridine by the standard method.[19] Irradiation of this in a 1:1 a mixture of benzene and methanol with Pyrex-filtered light under the standard procedure[19] gave 18-hydroxyiminopregnan-20α-ol **10** in 63% yield, together with ketone **6** (10%) and the parent 20α-ol **7** (4%) (Scheme 3).



Scheme 3 *Reagents and conditions:* i, NOCl–pyridine; ii, *hν* > 300 nm, benzene–MeOH; iii, $NaNO_2$–AcOH–aq. THF

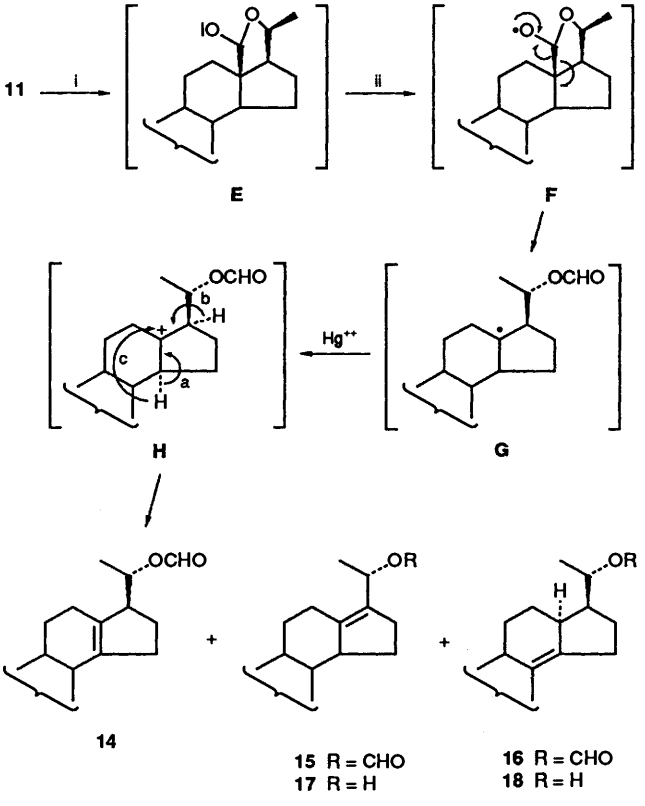
Although similar photoreaction of the 20β-ol nitrite **12** gave ketone **6** (9%) and the parent 20β-ol **8** (21%), the corresponding 18-hydroxyimino ketone **13** was obtained in only 12% yield (Scheme 4).



Scheme 4 *Reagents and conditions:* i, NOCl–pyridine; ii, *hν* > 300 nm, benzene–MeOH

The predominant formation of 18-hydroxyimino steroids in the photoreaction of steroidal 20α-nitrites, rather than in the photoreaction of the 20β-epimer, has repeatedly been reported,[20,21] and the results explained in terms of the smaller steric interaction between the 12β-hydrogen and the C-20 Me group in the 20α-isomer in the transition state.[21]

The 18-hydroxyiminopregnan-20α-ol **10** was then subjected to deoximation with sodium nitrite and acetic acid[22] in tetrahydrofuran (THF) to give a crystalline lactol **11** in 75% yield.



Scheme 5 *Reagents and conditions:* i, HgO–I_2, benzene; ii, *hν* > 300 nm

Irradiation of the hypoiodite (**E** in Scheme 5) of lactol **11**, prepared *in situ* by treatment with mercury(II) oxide (2 mol equiv.) and iodine in benzene by our standard method,[7] gave a mixture of isomeric 18-norpregnen-20α-ol formates (**14**, **15** and **16**) as outlined in Scheme 5. The formate **14**, obtained in 48% yield, was readily isolated by preparative TLC (PLC). High-resolution mass spectrometry indicated that the molecular formula is $C_{22}H_{32}O_3$. The anticipated reaction pathway (outlined in Scheme 5) together with the IR, ^1H NMR and mass spectral results (see Experimental section) indicated that the structure of formate **14** is 6β-methoxy-3α,5-cyclo-18-nor-5α-pregn-13-en-20α-yl formate. The formate **14** is formed from hypoiodite **E** *via* β-scission of the alkoxyl radical **F** at the carbon–carbon bond, followed by one-electron oxidation of the resulting carbon-centred radical **G** and removal of the 14α-proton (as outlined in Scheme 5).

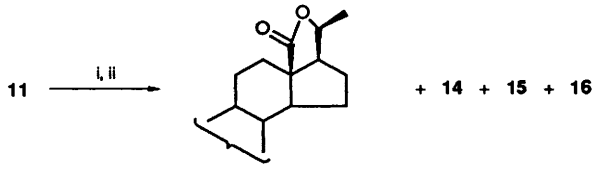
Two other minor formates (**15** and **16**) comprised a mixture, and were inseparable by PLC. They were therefore subjected to alkaline hydrolysis to produce two isomeric 18-norpregnen-20α-ols (**17** and **18**) in 3 and 5% yield. The molecular formula, $C_{21}H_{32}O_2$, was established for both formates **17** and **18** by high-resolution mass spectrometry. The ^1H NMR spectrum of product **17** exhibited a 1 H quartet at δ 4.70, assignable to the 20β-proton, in addition to three 3 H singlets due to 19-H_3, 21-H_3 and OMe protons. The chemical shift and the coupling

pattern of the 20β-proton, together with a consideration of its formation pathway, indicated that product **17** is 6β-methoxy-3α,5-cyclo-18-nor-5α-pregn-13(17)-en-20α-ol.

The ^{1}H NMR spectrum of product **18** exhibited a 1 H signal at δ 4.05 as a double quartet assignable to the proton attached to a carbon bearing a hydroxyl group, and three 3 H singlets due to the 19-H_3, 21-H_3 and OMe protons. The spectrum also showed the absence of any olefinic proton. A tentative structure, 6β-methoxy-3α,5-cyclo-18-nor-5α-pregn-8(14)-en-20α-ol, for product **18** can accommodate the spectral results, together with the probable reaction path leading to it. The 1 H signal at δ 4.05 is thus assignable to 20β-H.

Formate **15** should be formed by removal of the 17α-proton from a cationic intermedate **H**, while formate **16** can be formed *via* 1,2-shift of the 14α-proton of the intermediate **H** followed by removal of the 8β-proton (Scheme 5).

Both the products and their yields in this β-scission of the hypoiodite of lactol **11** when pyridine was added to the solvent were then examined. The photoreaction of the hypoiodite of lactol **11** in benzene containing a small amount of pyridine (2.5 mol equiv. of the substrate steroid) under conditions otherwise similar to those mentioned above gave a new product, **19**, in 25% yield, together with formates **14** (33%), **15** (14% after hydrolysis to the 20β-ol **17**) and **16** (10% after hydrolysis to the 20α-ol, **18**) (Scheme 6). The mass spectrometric and combustion



19

Scheme 6 *Reagents and conditions:* i, HgO–I_2, benzene–pyridine; ii, *hv* > 300 nm

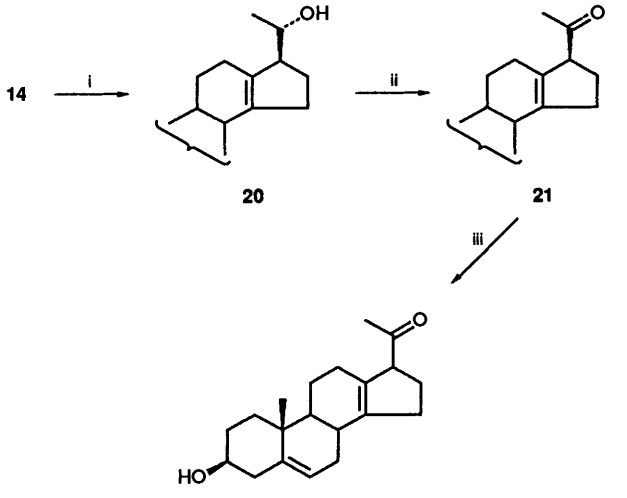
analysis results indicated that compound **19** had the molecular formula $C_{22}H_{32}O_3$. The IR spectrum exhibited a band assignable to the γ-lactone group. The ^{1}H NMR spectrum exhibited a 1 H double quartet at δ 4.66 with *J* 4.8 and 6.6 Hz, in addition to signals attributable to 19-H_3, 21-H_3 and OMe. These results indicate that the new product **19** is 6β-methoxy-18,20α-epoxy-3α,5-cyclo-5α-pregnan-18-one.

This experiment thus indicated that the addition of pyridine lowered the yield of formate **14**, which seemed to be a straightforward precursor leading to fukujusonorone, giving even more by-products.

The hydrolysis of formate **14** with potassium hydroxide in methanol gave the corresponding 20α-ol **20** in 85% yield. The spectral results were in full agreement with the assigned structure. The oxidation of the 20α-ol with pyridinium chlorochromate (PCC) in dichloromethane at room temperature gave crystalline 6β-methoxy-3α,5-cyclo-18-nor-5α-pregn-13-en-20-one **21** in 65% yield.

All attempts to oxidize the allylic 12-methylene group of the pregnene-20-one **21** to a carbonyl group under various published procedures were unsuccessful; the oxidation of the pregnene **21** with *tert*-butyl chromate in tetrachloromethane containing acetic acid and acetic anhydride at 60–65 °C,[23] with *tert*-butyl hydroperoxide in the presence of chromium hexacarbonyl [$Cr(CO)_6$] in refluxing acetonitrile,[24] with pyridinium dichromate (PDC) at 100 °C,[25] or with excess of sodium periodate and a catalytic amount of ruthenium trichloride and cetyltrimethylammonium bromide as the phase-transfer catalyst,[26] resulted in the formation of a complex mixture of products; oxidation of the pregnen-20-one **21** with isolated chromium trioxide (CrO_3)-pyridine complex in dichloromethane at room temperature,[27] or with a chromium trioxide–pyridine complex prepared *in situ* in refluxing dichloromethane in the presence of diphosphorus pentaoxide,[28] or with *tert*-butyl hydroperoxide and selenium dioxide in dichloromethane at 25 °C,[29] gave no oxidized product, and the starting material was recovered unchanged.

Finally, treatment of the masked 18-nor-5α-pregnen-20-one **21** with toluene-*p*-sulfonic acid (PTSA) in 1,4-dioxane by a standard method gave 12-deoxofukujusonorone, 3β-hydroxy-18-norpregna-5,13-dien-20-one **22** in 85% yield (Scheme 7).



22

Scheme 7 *Reagents and conditions:* i, KOH–aq.MeOH; ii, PCC–CH_2Cl_2; iii, TsOH–aq. 1,4-dioxane, reflux

The foregoing transformation of normal steroids into 18-norsteroids involving the selective β-scission of alkoxyl radicals generated from lactols under almost neutral conditions is additional confirmation that selective radical fragmentation is as useful as is ionic fragmentation in organic synthesis.

Experimental

M.p.s were determined using a Yanagimoto m.p. apparatus and are uncorrected. The IR spectra were determined for Nujol mulls with a JASCO IR 810 infrared spectrophotometer, unless stated otherwise. The ^{1}H NMR spectra were determined in $CDCl_3$ ($SiMe_4$ as internal reference) with a JEOL J-FX 270 spectrometer operating at 270 MHz, or with a Hitachi R-90H spectrometer operating at 90 MHz. The *J*-values are in Hz. The high- and low-resolution mass spectra were recorded with a JEOL JMS-DX 303 mass spectrometer at the Faculty of Pharmaceutical Sciences of this university. PLC was carried out on Merck silica gel 60 PF_{254}. The photolysis was carried out in a Pyrex tube with a 100-W high-pressure Hg arc lamp.

6β-Methoxy-3α,5-cyclo-5α-pregnan-20-one **6**.—3β-Hydroxypregn-5-en-20-one **5** (20.1 g, 63.5 mmol) and toluene-*p*-sulfonyl chloride (30.1 g, 2.5 mol equiv.) in pyridine (260 cm^3) were stirred for 24 h at room temperature. The solution was then poured into ice–water, and the crystals collected by filtration were dissolved in dichloromethane. The solution was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude tosate, which was dissolved in methanol (600 cm^3) containing potassium acetate (35 g). The solution was heated under reflux for 1 h and the solvent was removed by evaporation. Water was added to the residue; the reaction mixture was then extracted with diethyl ether and the extract was worked up in the usual way.

The product was recrystallized from methanol to give

cyclosteroid **6**[15] (16.8 g, 80%), m.p. 128–129 °C (Found: C, 79.7; H, 10.4. $C_{22}H_{34}O_2$ requires C, 79.95; H, 10.37%); ν_{max}/cm^{-1} 1705 (C=O) and 1097; δ(90 MHz) 0.67 (3 H, s, 18-H), 1.03 (3 H, s, 19-H_3), 2.11 (3 H, s, 21-H_3), 2.76 (1 H, t, $J \sim 3$, 6α-H) and 3.32 (3 H, s, OMe); *m/z* 330 (M^+, 26%), 315 [(M − Me)$^+$, 37], 298 [(M − MeOH)$^+$, 50], 275 (73) and 43 (100).

6β-*Methoxy*-3α,5-*cyclo*-5α-*pregnan*-20α- *and* 20β-*ol* **7** *and* **8** *by Reduction of Cyclosteroid* **6**.—(a) *With sodium and ethanol.* To a solution of cyclosteroid **6** (3.53 g, 10.7 mmol) in refluxing ethanol (350 cm^3) was added sodium (17.85 g, 776.1 mmol). The solution was heated under reflux until all of the sodium was consumed (TLC). To this solution was added sodium ethoxide [sodium (10.15 g, 441 mmol) in ethanol (50 cm^3)]; the solution was heated under reflux until all of the added sodium had reacted. Evaporation of the solvent gave a product, which was dissolved in diethyl ether. The ethereal solution was worked up in the usual way. The product was subjected to PLC [(3:1) benzene–diethyl ether] to give two 20-ols, **7** and **8**.

The less mobile alcohol was 20α-ol **7** (2.05 g, 58%), m.p. 99–102 °C (from acetone) (lit.,[15] a glass); ν_{max}/cm^{-1} 3500 (OH) and 1093; δ(90 MHz) 0.72 (3 H, s, 18-H_3), 1.02 (3 H, s, 19-H_3), 1.22 (3 H, d, *J* 6.2, 21-H_3), 2.77 (1 H, t, $J \sim 3$, 6α-H), 3.32 (3 H, s, OMe) and 3.71 (1 H, m, 20β-H).

The more mobile alcohol was 20β-ol **8** (1.04 g, 29%), m.p. 72–73.5 °C (from acetone) (lit.,[15] glass); ν_{max}/cm^{-1} 3322 (OH) and 1101; δ(90 MHz) 0.81 (3 H, s, 18-H_3), 1.03 (3 H, s, 19-H_3), 1.13 (3 H, d, *J* 6.2, 21-H_3), 2.77 (1 H, $J \sim 3$, 6α-H), 3.22 (3 H, s, OMe) and 3.71 (1 H, m, 20α-H).

(b) *With sodium borohydride.* To a solution of cyclosteroid **6** (102 mg, 0.309 mol) in ethanol (20 cm^3) was added sodium borohydride (13 mg, 0.344 mmol). The solution was stirred at room temperature for 90 h. Evaporation of the solvent gave a product, which was dissolved in diethyl ether. The solution was worked up in the usual way. The product was subjected to PLC [(3:1) hexane–ethyl acetate] to give a more mobile 20β-ol **8** (81 mg, 79%) and a less mobile 20α-ol **7** (13 mg, 13%).

18-*Hydroxyimino*-6β-*methoxy*-3α,5-*cyclo*-5α-*pregnan*-20α-*ol* **10** *by Photolysis of Cyclosteroid*-20α-*ol Nitrite* **9**.—To a solution of 20α-ol **7** (258 mg, 0.777 mmol) in pyridine was added dropwise a solution of nitrosyl chloride in pyridine until the colour of the solution became brown. The solution was stirred for 3 min at room temperature and was then poured into water–ice, and the crystals collected by filtration were dissolved in diethyl ether. The solution was worked up in the usual way. Evaporation of the solvent gave nitrite **9**, which was dissolved in a mixture of benzene (20 cm^3) and methanol (20 cm^3). The solution was irradiated with Pyrex-filtered light for 1 h at room temperature. After the solvent was removed, the product was subjected to PLC [(1:1) hexane–ethyl acetate] to give three products (**6**, **7** and **10**) in order of their mobility on TLC.

The most mobile product (26 mg, 10%) was the parent ketone **6**. The next mobile product (11 mg, 4%) was 20α-ol **7**. The most polar product **10** (178 mg, 63%) was *the* 18-*hydroxyimino*-*pregnan*-20α-*ol*, m.p. 155–156 °C (from hexane–dichloromethane) (Found: C, 73.1; H, 9.8; N, 3.8. $C_{22}H_{35}NO_3$ requires C, 73.09; H, 9.76; N, 3.87%); ν_{max}/cm^{-1} 3330 and 3200 (OH), 1099 and 930; δ(270 MHz) 1.00 (3 H, s, 19-H_3), 1.20 (3 H, d, *J* 2.57, 6β-OMe), 3.32 (3 H, s, OMe), 4.03 (1 H, m, 20β-H) and 7.56 (1 H, s, CH=N–); *m/z* 363 [(M + H_2),$^+$ 1.4%], 361 (M^+, 1.8), 344 [(M − OH)$^+$, 100], 329 [(M − MeOH)$^+$, 59] and 312 [(M − OH − MeOH)$^+$, 52].

Synthesis and Photoreaction of Cyclosteroid-20β-*ol Nitrite* **12**.—A solution of 20β-ol **8** (240 mg, 0.723 mmol) in pyridine (3 cm^3) was treated with nitrosyl chloride in pyridine as mentioned above to give nitrite **12**, which was dissolved in a mixture of dry benzene (18 cm^3) and metthanol (18 cm^3). The photolysis was carried out using a procedure similar to that for nitrite **9**, to give three products: **6**, **8** and *the* 18-*hydroxyiminopregnan*-20β-*ol* **13** (Found: M^+, 361.2624. $C_{22}H_{35}NO_3$ requires M, 361.2617); ν_{max}/cm^{-1} 3310 (OH); δ(270 MHz) 0.95 (3 H, s, 19-H_3), 1.14 (3 H, d, *J* 6, 21-H_3), 2.80 (1 H, t, *J* 3, 6α-H), 3.34 (3 H, s, 6β-OMe), 3.60 (1 H, m, 20α-H) and 7.52 (1 H, s, CH=N–); *m/z* 361 (M^+, 5.9%), 344 [(M − OH)$^+$, 100], 329 [(M − OH − Me)$^+$, 312 (56) and 306 (66).

6β-*Methoxy*-18,20α-*epoxy*-3α,5-*cyclo*-5α-*pregnan*-18-*ols* **11** *by Hydrolysis of Oxime* **10** *with Sodium Nitrite–Acetic Acid.*—To a solution of the 18-hydroxyiminopregnan-20α-ol **10** (566 mg, 1.57 mmol) in a mixture of THF (16 cm^3) and acetic acid (0.6 cm^3) was added a solution of sodium nitrite (1.88 g, 27.25 mmol) in water (10 cm^3). The solution was stirred for 22 h at room temperature and poured into water–ice. The crystals collected by filtration were dissolved in diethyl ether. The solution was worked up in the usual way. Removal of the solvent gave a product, which was purified by PLC [(2:1) hexane–ethyl acetate] to give *lactol* **11** (408 mg, 75%), m.p. 148–150 °C (from acetone) (Found: C, 76.1; H, 9.9. $C_{22}H_{34}O_2$ requires C, 76.26; H, 9.89%); ν_{max}/cm^{-1} 3392 (OH), 1108, 1092, 1060 and 1024; δ(270 MHz) 1.00 and 1.02 (each s, 19-H), 1.21 (d, *J* 6.23, 21-H_3), 2.81 (t, *J* 2.93, 6α-H), 3.34 (s, OMe), 4.3–4.5 (m, 20β-H) and 5.10 and 5.15 (each d, *J* 5.23 and 3.29, 18-H_2); *m/z* 348 [(M + H_2)$^+$, 0.3%], 347 [(M + H)$^+$, 1.7], 346 (M^+, 6.3), 331 [(M − Me)$^+$, 33.1], 314 [(M − MeOH)$^+$, 65.8], 291 (62.6), 268 (80.4) and 147 (100).

β-*Scission of Alkoxyl Radical generated from the Photolysis of Hypoiodite of Lactol* **11**.—(a) *In benzene.* To a solution of lactol **11** (287 mg, 0.829 mmol) in benzene (40 cm^3) were added mercury(II) oxide (359 mg, 1.66 mmol) and iodine (421 mg, 1.66 mmol). The solution was flushed with nitrogen and irradiated with Pyrex-filtered light for 7 h at room temperature. The solution was filtered, and the organic layer of the filtrate was washed successively with 5% aq. sodium thiosulfate, water and brine, and dried over anhydrous sodium sulfate. Removal of the solvent gave a product, which was subjected to PLC [(3:1) hexane–ethyl acetate], resulting in two fractions (A and B). The more mobile fraction (A) was a mixture of products. The less mobile fraction (B) gave 6β-*methoxy*-3α,5-*cyclo*-18-*nor*-5α-*pregn*-13-*en*-20α-*yl formate* **14** as a glass (138 mg, 48%) (Found: M^+, 344.2357. $C_{22}H_{32}O_3$ requires *M*, 344.2352); ν_{max}(neat)/cm^{-1} 1719 (C=O), 1193 and 1096; δ(270 MHz) 1.02 (3 H, s, 19-H_3), 1.33 (3 H, d, *J* 6.2, 21-H_3), 2.78 (1 H,t, *J* 2.6, 6α-H), 3.32 (3 H, s, OMe), 5.28 (1 H, m, 20β-H) and 8.04 (1 H, s, OCHO); *m/z* 344 (M^+, 22%), 307 (40), 298 [(M − HCOOH)$^+$, 10], 284 (18), 266 (14), 248 (16) and 216 (100).

Fraction A (37 mg) was stirred and hydrolysed with potassium hydroxide (5%) in methanol (5 cm^3) at room temperature for 1 h. After the solvent had been evaporated off, the residue was dissolved in diethyl ether. The solution was washed successively with dil. hydrochloric acid, water and brine, and dried over anhydrous sodium sulfate. The product was again subjected to PLC [(2:1) hexane–ethyl acetate] to give two fractions (A_1 and A_2). The less mobile fraction (A_2) gave 6β-*methoxy*-3α,5-*cyclo*-18-*nor*-5α-*pregn*-13(17)-*en*-20α-*ol* **17** (7 mg, 3%) as a glass (Found: M^+, 316.2415. $C_{21}H_{32}O_2$ requires *M*, 316.2402); ν_{max}(neat)/cm^{-1} 3390 (OH) and 1090; δ(270 MHz) 0.96 (3 H, s, 19-H_3), 1.24 (3 H, d, *J* 6.6, 21-H_3), 2.79 (1 H, t, $J \sim 3$, 6α-H), 3.31 (3 H, s, 6β-OMe) and 4.70 (1 H, q, *J* 6.6, 20β-H).

The more mobile fraction gave an *isomeric* 20α-*ol* **18** as a glass (12 mg, 5%), tentatively assigned as the 8(14)-ene (Found: M^+, 316.2421); ν_{max}/cm^{-1} 3412 (OH) and 1096; δ(270 MHz) 1.01 (3 H, s, 19-H_3), 1.16 (3 H, d, $J \sim 3$, 21-H_3), 3.34 (3 H, s, 6β-OMe) and 4.05 (1 H, dq, *J* 6.2 and 2.2, 20β-H); *m/z* 316 (M^+, 0.25%),

298 [(M − H_2O)$^+$, 1.02], 284 [(M − MeOH)$^+$, 20], 266 [(M − H_2O − MeOH)$^+$, 8] and 239 (100).

(b) *In benzene containing pyridine.* To a solution of lactol **11** (102 mg, 0.295 mmol) in benzene (16 cm^3) containing pyridine (0.06 cm^3, 0.743 mmol, 2.52 mol equiv.), were added mercury(II) oxide (135 mg, 0.623 mmol) and iodine (160 mg, 0.630 mmol). The solution was flushed with nitrogen and irradiated for 4 h.

Separation of the products by PLC, as mentioned above, gave three fractions (A, B and C). Fraction A (27 mg) was a mixture of the products. Fraction B (25 mg, 25%) gave *lactone* **19**, m.p. 164–165 °C (from acetone) (Found: C, 76.7; H, 9.35. $C_{22}H_{32}O_3$ requires C, 76.70; H, 9.36%); ν_{max}/cm^{-1} 1753 (C=O), 1269, 1171, 1123 and 1086; δ(270 MHz) 1.09 (3 H, s, 19-H_3), 1.36 (3 H, d, *J* 6.6, 21-H_3), 2.78 (1 H, t, *J* 2.9, 6α-H), 3.31 (3 H, s, OMe) and 4.66 (1 H, dq, *J* 4.8 and 6.6, 20β-H); *m/z* 344 (M$^+$, 39%), 329 [(M − Me)$^+$, 55], 312 [(M − MeOH)$^+$, 82], 289 (100), 105 (38) and 91 (47). Fraction C gave formate **14** (33 mg, 33%).

Fraction A was subjected to hydrolysis: to a solution of fraction A (33 mg) in methanol (3.2 cm^3) was added aq. potassium carbonate (20 mg, 0.15 mmol in 1 cm^3). The solution was stirred for 1.5 h at room temperature. After the mixture had been evaporated, the product was extracted with diethyl ether. The extract was worked up in the usual way to give a mixture of products. The mixture was subjected to PLC [(3:1) hexane–ethyl acetate], resulting in two products. The more mobile product (13 mg, 14%) was identified as being compound **17**. The less mobile product (9 mg, 10%) was identical with product **18**.

6β-*Methoxy*-3α,5-*cyclo*-18-*nor*-5α-*pregn*-13-*en*-20α-*ol* **20** *by Hydrolysis of the* 18-*Norpregn*-13-*en*-20α-*yl Formate* **14**.—Formate **14** (138 mg, 0.401 mmol) was dissolved in methanol containing 5% potassium hydroxide. The solution was stirred for 2 h at room temperature. After removal of the solvent, the residue was dissolved in diethyl ether. The solution was then washed successively with dil. hydrochloric acid, water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave crude 20α-ol **20**, which was subjected to PLC [(2:1) hexane–ethyl acetate] to give pure 20α-*ol* **20** (108 mg, 85%) as a glass (Found: M$^+$, 316.2373. $C_{21}H_{32}O_2$ requires *M*, 316.2402): ν_{max}(neat)/cm^{-1} 3376 (OH) and 1098; δ(270 MHz) 1.03 (3 H, s, 19-H_3), 1.14 (3 H, d, *J* 6.6, 21-H_3), 2.79 (1 H, t, *J* ~ 3, 6α-H), 3.32 (3 H, s, OMe) and 4.28 (1 H, dq, *J* 6.6 and 1.47, 20β-H); *m/z* 316 (M$^+$, 30%), 284 [(M − MeOH)$^+$, 22], 279 (31) and 216 (100).

6β-*Methoxy*-3α,5-*cyclo*-18-*nor*-5α-*pregn*-13-*en*-20-*one* **21** *by Oxidation of the* 18-*Norpregn*-13-*en*-20α-*ol* **20**.—To a solution of the 20α-ol **20** (218 mg, 0.690 mmol) in dichloromethane (5 cm^3) was added a solution of PCC (148 mg, 0.688 mmol) in dichloromethane (8 cm^3). The solution was stirred for 17 h at room temperature. After addition of diethyl ether to the solution, the mixture was filtered. The filtrate was worked up in the usual way to give the crude *ketone* **21** (141 mg, 65%), m.p. 105–106 °C (from acetone–water) (Found: M$^+$, 314.2260. $C_{21}H_{30}O_2$ requires *M*, 314.2246); ν_{max}/cm^{-1} 1690 (C=O) and 1099; δ(270 MHz) 1.04 (3 H, s, 19-H_3), 2.17 (3 H, s, 21-H_3), 2.65 (1 H, t, *J* 9.9, 17α-H), 2.76 (1 H, t, 2.6, 6α-H), 3.12 (1 H, d, *J* 1.1) and 3.29 (3 H, s, OMe); *m/z* 314 (M$^+$, 30%), 300 (13), 282 [(M − MeOH)$^+$, 14], 277 (37) and 43 (100).

3β-*Hydroxy*-18-*norpregna*-5,13-*dien*-20-*one* **22** (12-*Deoxofukujusonorone*).—To a solution of the masked 18-norsteroid **21** (68 mg, 0.22 mmol) in 1,4-dioxane (4 cm^3) was added a solution of PTSA (8 mg, 0.042 mmol) in water (3 cm^3). The solution was heated at 80 °C for 1 h, and then poured into water–ice (10 cm^3). The mixture was extracted with diethyl ether three times. The combined extracts were worked up in the usual way to give crude 12-deoxofukujusonorone. The product was purified by PLC [(1:1) hexane–ethyl acetate] to give pure 12-*deoxofukujusonorone* **22** (55 mg, 85%), m.p. 130–131 °C (from hexane–dichloromethane) (Found: M$^+$, 300.2073. $C_{20}H_{28}O_2$ requires *M*, 300.2089); ν_{max}/cm^{-1} (KBr) 3300 (OH), 1682 (C=O), 1182, 1054 and 843; δ(270 MHz) 1.02 (3 H, s, 19-H_3), 2.17 (3 H, s, 21-H_3), 2.64 (1 H, t, *J* ~ 10, 17α-H), 3.46–3.58 (1 H, m, 3α-H) and 5.34 (1 H, d, *J* 5, 6-H); *m/z* 300 (M$^+$, 57%), 285 [(M − Me)$^+$, 21], 257 [(M − CH_3CO)$^+$, 31], 239 [(M − MeCO − H_2O)$^+$, 40], 84 (88) and 43 (100).

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