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Replacement of an 11-Carbonyl Group of 11-Oxo Steroid by an Oxygen Atom. A New Partial Synthesis of 11-Oxaprogesterone[1)]

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We describe the transformation of commercially available 3α-hydroxy-5β-pregnane-11,20-dione acetate (**1**) into 11-oxaprogesterone (**15**) in 11 steps including the regioselective β-scission of an alkoxyl radical as a key step.

Among oxamodification of steroids, the synthesis of 11-oxasteroids has been extensively investigated by Engel and his colleagues. In 1968 they achieved the transformation of hecogenin into the first oxasteroid, 11-oxaprogesterone (**15**) having a significant biological activity, in 22 steps.[2,3)] They have also reported the synthesis and biological evaluation of several related 11-oxasteroids.[4,5)] Recently, the partial synthesis of 11-oxaestradiol via dye-sensitized photooxygenation of a 3-hydroxy-1,3,5(10),9-estratetraen-17-one methyl ether has also been reported by Bonet and his colleagues.[6)]

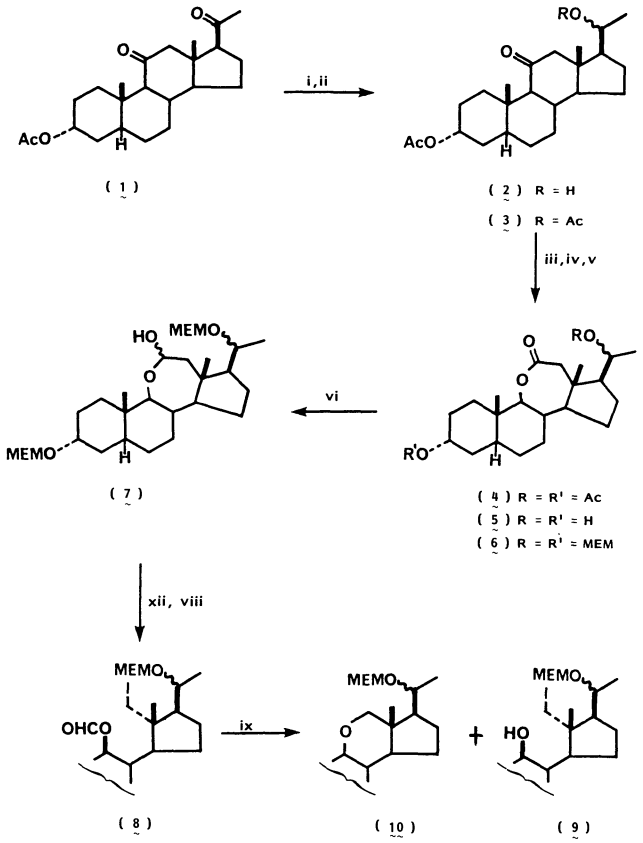
We ourselves have reported new general methods for transforming steroidal five- and six-membered cyclic alcohols or cyclic ketones as starting materials into oxasteroids with the same ring size in 2 or 4 steps[7–9)] and synthesized 1-oxa-, 3-oxa-, 4-oxa-, 6-oxa-, 7-oxa-, 16-oxa-, and 17-oxasteroids effectively by these methods. We have also recently shown that the synthesis of 11-oxasteroids can be achieved by our general method by which cyclic ketones are transformed into the corresponding cyclic ethers and that the synthesis of 11-oxa-5β-pregnan-3α-ol can be achieved by the replacement of the 11-carbonyl group of a commercially available 3α-hydroxy-5β-pregnane-11,20-dione acetate (**1**).[10)]

We wish to describe here the partial synthesis of 11-oxaprogesterone (**15**) from pregnane dione **1** based on our method by which cyclic ketones are transformed into cyclic ethers.

Results

A selective reduction of the 20-carbonyl group of a commercially available pregnane derivative **1** with $NaBH_4$ at room temperature followed by acetylation by the standard method gave a mixture of 3α,20α- and 3α,20β-dihydroxy-5β-pregnan-11-one 3,20-diacetate (**3**) in 94% yield. The preparations of this mixture of epimers by the reduction of 5β-pregnane-3,11,20-trione or 3α-hydroxy-5β-pregnane-11,20-dione with $NaBH_4$ followed by acetylation,[11,12)] have been reported to give the 20β-epimer as the predominant product.[12)]

A Baeyer–Villiger oxidation of diacetates **3** with potassium peroxodisulfate in glacial acetic acid containing concd sulfuric acid for 10 days at room temperature led to a regio- and stereoselective oxidation of the carbonyl group and gave a crystalline mixture of 3α,20α- and 3α,20β-dihydroxy-11-oxa-*C*-homo-5β-pregnane-12-one 3,20-diacetate (**4**) in a 56% yield. The ratio of the 20β-isomer and 20α-isomer was estimated to be approximately 1.7:1 based on the area ratio of the signals due to the two 9α-protons of the



Scheme 1. Reagents: i) $NaBH_4$, EtOH, 20°C, 5 h; ii) $(CH_3CO)_2O$, pyridine, 35 h; iii) AcOH, concd H_2SO_4, $K_2S_2O_8$, 20°C, 10 d; iv) aq MeOH, Na_2CO_3, reflux, 18 h; v) CH_3CN, MEM·NH_4Cl, 16 h; vi) toluene, DIBAL, 20°C, 1 d; vii) HgO, I_2, benzene, 20°C; viii) *hν*, 20°C, 4 h; ix) THF, $NaBH_4$, reflux, 1 d.

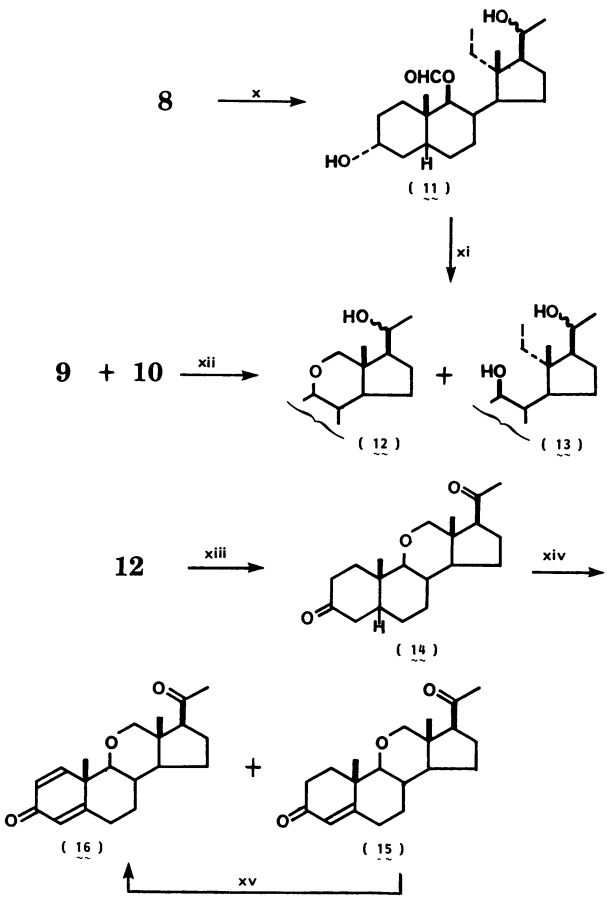
^{1}H NMR spectrum. To the best of our knowledge, no successful formation of lactones from 11-oxosteroids by means of the Baeyer-Villiger oxidation has previously been reported and the present example seems to be the first one. Examination of the oxidation product by means of TLC indicated that neither 9β-isomers nor 12-oxa-isomers of lactones **4** were present in the product. Its ^{1}H NMR spectrum exhibited two clear doublets at δ 4.27 and 4.38 with J=9.62 and 10.62 arising from the 9α-H of the 20-isomers.

Before transforming the lactone **4** into the corresponding lactols, the replacement of the 3α- and 20-acetyl groups by an MEM† group was necessary. The diacetate was therefore treated with sodium carbonate in aq methanol under reflux for 18 h to give the corresponding diol **5** in a 78% yield. The ratio of the two isomers with regard to the 20 position was 1:1.5. The treatment of diols **5** with [(2-methoxyethoxy)-methyl]triethylammonium chloride in acetonitrile under reflux for 16 h gave the corresponding MEM ether **6** in 76% yield. The dihydroxylactones protected by the MEM group was then transformed into the corresponding lactols **7** in a 73% yield by a treatment with DIBAL†† in toluene for one day at room temperature. The lactols **7** were then subjected to a regioselective homolytic cleavage of the 12,12a-carbon-carbon bond according to the procedure reported previously;[8] the lactols **7** in benzene were first transformed into the corresponding hypoiodite with 3 molar equivalents each of mercury(II) oxide and iodine and the solution was irradiated with a 100-W Hg arc for 4 h through a Pyrex to give iodo formates **8** in a 73% yield. Signals due to the formyloxy groups of the 20α-isomer and 20β-isomer in the ^{1}H NMR spectrum appeared at δ 8.23 and 8.33 as two singlets. The ratio of the two epimers estimated by the area ratio of these two singlets was 1:1.6.

The first attempt to cyclize the iodo formates **8** into the corresponding oxasteroids was made by heating the formates **8** in THF with $NaBH_4$ under reflux for 2 days. This procedure resulted, however, in only a low yield of oxasteroid **10** with an accompanying formation of 11β-ol **9** arose from hydrolysis. The crude oxasteroid **10**, isolated by means of preparative TLC, was immediately subjected to the removal of the protecting MEM group to give a mixture of 11-oxa-5β-pregnane-3α,20α- and 3α,20β-diol (**12**) by the standard method. The overall yield of oxasteroids **12** from iodo formates **8** was only 16%.

We obtained a much higher yield of oxasteroids **12**, however, by the initial removal of the MEM group of iodo formates **8** to iodo formates **11** followed by cyclization, although the intramolecular displacement of the iodo formates **8** in dichloromethane with $TiCl_4$ at room temperature gave a mixture of two epimers of iodo formates **11** in a 96% yield. The ratio of the two epimers estimated by the signal areas due to their 9α-H in the ^{1}H NMR was 1.1:1. The heating of iodo formates **11** in THF under reflux for 3 days gave a mixture of 11-oxa-5β-pregnane-3α,20α- and 3α,20β-diol (**12**) in a 51% yield with an accompanying formation of triols **13**.

Oxidation of 20-epimers of dihydroxyoxasteroids **12** in dichloromethane with PCC††† gave 11-oxa-5β-pregnane-3,20-dione (**14**) in a 84% yield. Further oxidation of dione **14** in dioxane with DDQ afforded 11-oxaprogesterone (**15**) and 11-oxapregna-1,4-diene-3,20-dione **16** in 11% and 31% yields. The transformation of the latter into the former by means of selective homogeneous hydrogenation with tris(triphenylphosphine)chlororhodium as a catalyst has already been achieved in 85% yield by Engel and his colleagues.[2]



Scheme 2. Reagents: x) CH_2Cl_2, $TiCl_4$, 0°C, 20 min; xi) THF, $NaBH_4$, reflux, 3 d; xii) CH_2Cl_2, $TiCl_4$, 0°C, 40 min; xiii) CH_2Cl_2, PCC, 0°C, 12 h; xiv) dioxane, DDQ, reflux, 23 h; xv) benzene, H_2, $(Ph_3P)_3RuCl$, 20°C, 5 h.

† MEM; (2-methoxyethoxy)methoxy.

†† DIBAL; diisobutylaluminium hydride.

††† PCC; pyridinium chlorochromate.

Experimental

Mps were recorded with a Yanagimoto micro mp apparatus and are uncorrected. IR spectra were determined for Nujol mull with a JASCO IR 810 infrared spectrophotometer. ^{1}H NMR spectra were determined with JEOL JNM-FX 270 high-resolution FT-NMR spectrometer (270 MHz) (Solvent $CDCl_3$; $SiMe_4$ as internal standard) (Faculty of Pharmaceutical Sciences of this University). TLC was carried out on a Merck Kieselgel 60 PF_{254}. The high- and low-resolution mass spectra were determined with a JEOL JMA-D 300 spectrometer (70 eV) (Faculty of Agriculture or Faculty of Pharmaceutical Sciences of this University). Optical rotations were measured with a JASCO DIP-360 digital polarimeter.

3α,20α- and 3α,20β-Dihydroxy-5β-pregnan-11-one 3,20-Diacetates (3). Commercially available 3α-hydroxy-5β-pregnane-11,20-dione 3-acetate (**1**) (5 g) in ethanol (350 ml) was reduced with $NaBH_4$ (1 g) at room temperature for 5 h by the standard procedure to yield a mixture of 3α,20α- and 3α,20β-dihydroxy-5β-pregnan-11-one 3-acetates (**2**). The crude 20-ols **2** were immediately acetylated with acetic anhydride (25 ml) and pyridine (50 ml) for 35 h at room temperature. The solution was poured into water and the crystals were collected by filtration, washed with water and dissolved in dichloromethane. The solution was worked up in the usual way to yield 3,20-diacetates **3** (5.94 g). Recrystallization of the diacetates with hexane–ethyl acetate gave a stereoisomeric mixture of 3,20-diacetates **3** (5.24 g, 94%). Mp 161.5—163.0 °C (lit,[11] 160.5—161.0 °C)

Baeyer-Villiger Oxidation of 3α,20α-Dihydroxy-5β-pregnan-11-one 3,20-Diacetates. The diacetates (1.59 g), potassium peroxodisulfate (7 g) and concd sulfuric acid (7 ml) in glacial acetic acid (39 ml) in a vessel covered by aluminum foil was set aside for 10 days at room temperature. The reaction mixture was extracted with chloroform (ca. 40 ml× 5). The combined extracts were washed with 5% aqueous sodium thiosulfate, brine and water and dried over $MgSO_4$. The work-up of the solution gave a residue which was subjected to preparative TLC with 1:1 hexane–ethyl acetate to yield two fractions. The less polar fraction (1.06 g) was the starting material. The more polar fraction (300 mg) was a crude lactone **4** which was recrystallized from hexane–ethyl acetate. Mp 192—195 °C. (Found: M$^+$, 434.2676. $C_{25}H_{38}O_6$ requires M, 434.2668); IR 1727 (OAc and lactone C=O), 1244 and 1039 cm^{-1}; ^{1}H NMR δ=0.75 (3H, s, 18-H of 20α- and 20β-isomer), 1.08 (s, 19-H of 20α- and 20β-isomer), 1.17 (d, J=5.86 Hz, 21-H), 2.03 (s, OAc of 20α-isomer), 2.04 (s, OAc of 20β-isomer), 2.10 (s, OAc of 20β-isomer), 2.14 (s, OAc of 20α-isomer), 2.39 and 2.66 (each d, J=14.2 Hz, 12a-H of 20α-isomer), 2.51 and 3.22 (each d, J=13.9 Hz, 12a-H of 20β-isomer), 4.27 (d, J=9.52 Hz, 9aα-H of 20β-isomer), 4.38 (d, J=10.62 Hz, 9α-H of 20α-isomer), and 4.77 (m, 3β-H and 20-H of 20α- and 20β-isomers). EIMS m/z 434 (M$^+$, 4.8%). 374 [(M−CH_3CO_2H)$^+$, 11.4], 324 [(M−2CH_3COOH)$^+$, 18.6], and 43 (100).

3α,20α- and 3α,20β-Dihydroxy-5β-C-homo-11-oxapregnan-12-one (5). To the lactone **4** (270 mg) in methanol (20 ml), aq. saturated sodium carbonate (2 ml) was added. The solution was heated under reflux for 18 h. The removal of the solvent gave a residue which was dissolved in dichloromethane, then washed with a 5% hydrochloric acid, brine and water and dried over $MgSO_4$. The usual work-up gave a product (223 mg) which was purified by means of preparative TLC with ethyl acetate to give diol **5** as an amorphous solids (169 mg, 78%). (Found: M$^+$, 350.2471. $C_{21}H_{34}O_4$ requires M, 350.2457); IR 3380 (OH), 1708 (lactone C=O) and 1041 cm^{-1} (C-O-C); ^{1}H NMR δ=0.87 (s, 18-H of 20α-isomer), 0.93 (s, 18-H of 20β-isomer), 1.06 (s, 19-H of 20β-isomer), 1.07 (s, 19-H of 20α-isomer), 1.00 (d, J=6.23 Hz, 21-H of 20β-isomer), 1.16 (d, J=6.23 Hz, 21-H of 20α-isomer), 2.46 and 3.61 (each d, J=13.6 Hz, 12a-H of 20α-isomer), 2.52 and 3.26 (each d, J=13.6 Hz, 12a-H of 20β-isomer), 3.70 (2H, m, 3β-H and 20α- and 20β-H), 4.30 (d, J=9.89 Hz, 9α-H of 20α-isomer), and 4.40 (d, J=9.89 Hz, 9α-H of 20α-isomer); EIMS m/z 350 (M$^+$, 18.9), 322 [(M−H_2O)$^+$, 51.4], 341 [(M−2H_2O)$^+$, 50.0], and 81 (100%).

3α,20α- and 3α,20β-Dihydroxy-5β-C-homo-11-oxapregnan-12-one 3,20-MEM Ether (6). To diol **5** (163 mg) in dry acetonitrile (10 ml), MEM triethylammonium chloride (400 mg) was added. The solution was heated under reflux for 16 h and the solvent was removed under vacuum. The residue was dissolved in dichloromethane–acetone. The solution was washed with aq 5% sodium hydrogencarbonate, brine and then water and dried over $MgSO_4$. The usual work-up gave a crude MEM ether. Since the IR spectrum indicated the presence of the starting diol in this product, the crude MEM ether was again subjected to the above procedure to transform the starting diol into MEM ether. The product was purified by means of preparative TLC with ethyl acetate to give oily MEM ether **6** (187 mg, 76.3%). (Found: M$^+$, 526.3493. $C_{29}H_{50}O_8$ requires M, 526.3503); IR 1735 (lactone C=O), 1119 (C-O-C) and 1048 cm^{-1} (C-O-C); ^{1}H NMR δ=0.80 (s, 18-H of 20α-epimer), 0.83 (s, 18-H of 20β-epimer), 1.05 (s, 19-H of 20α-epimer), 1.06 (s, 19-H of 20β-epimer), 3.38 (s, OMe), 3.39 (s, OMe), 3.56—3.74 (m, -OCH_2CH_2O-), 4.28 (d, J=9.80 Hz, 9α-H of 20β-epimer), 4.38 (d, J=9.80 Hz, 9α-H of 20β-isomer), and 4.68—4.89 (4H, m, -OCH_2O-), EIMS: m/z 526 (M$^+$, 0.1), 89 (95.6), and 59 (100%).

Reduction of 3α,20α- and 3α,20β-Dihydroxy-5β-C-homo-11-oxapregnan-12-one 3,20-MEM Ether (6) with DIBAL. To lactone MEM ether **6** (195 mg) in dry toluene (10 ml), a DIBAL solution (0.53 ml) (1 M in toluene) was added dropwise at −78 °C in an atmosphere of nitrogen. The solution was stirred for 1 day at room temperature. After the solution had again been cooled to −78 °C, a more DIBAL solution (0.2 ml) was added and the solution stirred for 4 h at room temperature. The reaction was quenched by the addition of iced water and the solution was filtered. After the addition of chloroform and acetone, the solution was washed with brine and then with water and dried over $MgSO_4$. The usual work-up gave a product which was purified by means of preparative TLC with ethyl acetate to give only lactol **7** (143 mg, 73%). [Found: (M−H_2O)$^+$, 510.3573. $C_{29}H_{50}O_7$ requires M, 510.3557]: IR 3442 (OH), 1099 (C-O-C) and 1043 cm^{-1} (C-O-C); ^{1}H NMR δ=3.85 (d, J=9.52 Hz, 9α-H of 20α-epimer), 3.97 (d, J=9.65 Hz, 9α-H of 20α-epimer), 5.14 (m, 12-H of 20β-epimer), and 5.33 (m, 12-H of 20α-epimer); EIMS m/z 510 [(M−H_2O)$^+$, 0.19] and 59 (100%).

Preparation of 3α,20α- and 3α,20β-Bis[3-(2-methoxyethoxy)methoxy]-11-iodo-9,11-seco-C-nor-5β-yl Formates (8). Lactol **7** (155 ml) was dissolved in dry benzene (20 ml) containing pyridine (0.2 ml). To this solution mercury(II) oxide (200 mg) and iodine (230 mg) were added. The solution was then flashed with nitrogen and irradiated with a

100-W high-pressure Hg arc for 4 h. The solution was then filtered and the filtrate was washed with aq 5% sodium thiosulphate, brine and then water successively and dried over $MgSO_4$. The usual work-up of the solution gave a residue (193 mg) which was subjected to preparative TLC with a 1:2 hexane–ethyl acetate. The most mobile fraction (140 mg, 73%) was two 20-epimers of iodo formates **8**. IR 1721 (OCHO) and 1025—1175 (C-O-C); ^{1}H NMR δ= 0.93 (s, 18-H of 20α-epimer), 0.95 (s, 18-H of 20β-epimer), 1.04 (s, 19-H of 20α-epimer), 1.06 (s, 19-H of 20α-epimer), 3.39 (s, OMe), 3.51—3.78 (m, $-OCH_2CH_2O-$), 4.74—4.81 (m, $-OCH_2O-$), 5.21 (d, J=10.99 Hz, 9α-H of 20β-epimer); 5.32 (d, J=9.16 Hz, 9α-H of 20α-epimer), 8.23 (s, OCHO of 20α-epimer), and 8.33 (s, OCHO of 20β-epimer); EIMS: m/z 549 [(M−OMEM)$^+$, 0.14], 397 (2.1), 89 (100), and 59 (80.1%).

Preparation of 3α,20α- and 3α,20β-Dihydroxy-11-iodo-9,11-seco-*C*-nor-5β-pregnan-9β-yl Formate (11). To iodo formate **8** (50 mg) in dichloromethane (3 ml), titanium tetrachloride (0.2 ml) was slowly added at 0 °C. After the solution had been stirred for 20 min at 0 °C, concd aq ammonia was added. The combined organic layers were washed with brine and then with water and dried over $MgSO_4$. The usual work-up gave an oily product (50 mg) which was purified by means of preparative TLC with ethyl acetate to give amorphous formate **11** (35 mg, 96%). [Found: (M−HI−H_2O)$^+$, 332.2321, $C_{21}H_{32}O_3$ requires M 332.2351]; IR ($CHCl_3$) 3410 (OH), 1719 and 1189 (-OCHO); ^{1}H NMR δ=5.20 (d, J=10.99 Hz, 9α-H), 5.30 (d, J=10.99 Hz, 9α-H), 8.30 (s, OCHO), and 8.35 (s, OCHO); EIMS m/z 415 [(M−OCHO−H_2O)$^+$, 0.22], 332 [(M−HI−H_2O)$^+$, 2.8], 305 [(M−HCHO−I)$^+$, 2.3], 287 [(M−OCHO−H_2O)$^+$, 84.3], 269 [(M−HCHO−I−2H_2O)$^+$, 56.4], and 95 (100%).

11-Oxa-5β-pregnane-3α,20α and 3α,20β-diol (12). To iodo formates **11** (90 mg) in dry THF (10 ml), $NaBH_4$ (180 mg) was added and the solution was heated under reflux for 3 days. The removal of the solvent gave a residue which was dissolved in dichlorormethane. The solution was washed with brine and then with water and dried over anhydrous $MgSO_4$. The usual work-up of the solution gave a product (80 mg) which was subjected to preparative TLC with a 2:1 ethyl acetate–hexane to give three fractions. The most mobile fraction (10 mg) was the starting iodo formates **11**. The next mobile fraction (31 mg, 51%) was the amorphous epimers **12** of oxasteroid. (Found: M$^+$, 322.2523. C_{20}-$H_{34}O_3$ requires M, 322.2508); IR 3280 (OH), 1114, 1085, and 1072 cm^{-1}; ^{1}H NMR δ=(the predominant epimer of the 20α- and 20β-isomers), 0.86 (3H, s, 18-H), 1.02 (3H, s, 19-H), 3.12 (1H, d, J=9.89 Hz, 9α-H), 3.18 (1H, d, J=10.63 Hz, 12-H), 3.61—3.75 (2H, m, 3β-H and 20ξ-H) and 4.15 (1H, d, J=10.63 Hz, 12-H).

The most polar fraction (30 mg, 35%) was an oily 11-iodo-*C*-nor-9,10-seco-5β-pregnane-3α,9β,20α- and 3α,9β,20β-triols. IR ($CHCl_3$) 3392 (OH) and 1094 cm^{-1} (C-O); ^{1}H NMR δ=3.04 (d, J=10.63 Hz, 11-H), 3.34 (d, J=9.90 Hz, 9α-H); 3.56—3.74 (m, 3α-H, 11-H, 20α-H, and 20β-H); the epimer, δ=3.26 (d, J=10.26 Hz, 11-H), 3.77 (d, J=10.26 Hz, 11-H), and 3.94 (d, J=9.90 Hz, 9α-H), ^{1}H NMR m/z 433 (0.27), 415 (1.08), 397 (0.68), 322 [(M−HI)$^+$, 36.1], 304 [(M−HI−H_2O)$^+$, 35.4], and 44 (100%).

Preparation of 11-Oxa-5β-pregnane-3,20-dione (14). To diol **13** (30 mg) in dichloromethane (5 ml), PCC (100 mg), and Celite (100 mg) were added at 0 °C and the solution was stirred for 12 h at room temperature. After the addition of diethyl ether, the solution was filtered. The removal of the solvent from the filtrate gave a residue which was purified by means of preparative TLC with a 2:3 hexane–ethyl acetate to give crystals of dione **14** (25 mg, 84%). The specimen for analysis was obtained by recrystallization from hexane–ethyl acetate. Mp 153.5—155.0 °C. (Found: C, 75.47; H, 9.60%. $C_{20}H_{30}O_3$ requires C, 75.43; H, 9.50%); $[\alpha]_D^{22}$ +48° (c 1, $CHCl_3$); IR 1715 and 1703 (C=O), 1078 and 1071 (C-O-C); ^{1}H NMR δ=0.77 (3H, s, 18-H), 1.10 (3H, s, 19-H), 2.07 (3H, s, 21-H), 3.26 (1H, d, J=9.53 Hz, 9α-H), 3.47 (1H, d, J=10.26 Hz, 12-H), and 4.16 (1H, d, J=10.26 Hz); EIMS: m/z 318 (M$^+$, 52.2), 300 (6.9), 288 (9.9), 233 (37.4), and 43 (100%).

Preparation of 11-Oxa-5β-pregnane-3,20-dione (14) from Iodo Formate 8 via 10 and 12. Iodo formate **8** (139 mg) in dry THF (6 ml) containing $NaBH_4$ (139 mg) was heated under reflux for 1 day in an atmosphere of dry nitrogen. To the solution a further amount (50 mg) of $NaBH_4$ was added and the solution was heated under reflux for 1 day. After the removal of the solvent the residue was dissolved in dichloromethane. The solution was washed with brine and then with water and dried over anhydrous $MgSO_4$. The removal of the solvent gave an oily product (120 mg) which was subjected to preparative TLC with a 1:1 hexane–ethyl acetate to give an oily product (80 mg). To the product in dichloromethane (5 ml), titanium tetrachloride (0.28 ml) was added and the solution was stirred for 40 min at 0 °C. To the solution concd aq ammonia was added and the organic layer was washed with brine and then with water and dried over anhydrous $MgSO_4$. The usual work-up of the solution gave a product (60 ml) which was subjected to preparative TLC with a 1:2 hexane–ethyl acetate to give oxasteroid **12** (15 mg) and triol **13** (35 mg). Oxasteroid **12** was oxidized with PCC to give a new dione **14** (11 mg) as described previously. The overall yield from **8** to **12** was 16%.

Synthesis of 11-Oxaprogesterone (15) and 11-Oxapregna-1,4-diene-3,20-dione (16). 11-Oxasteroid **14** (28 mg) in dry dioxane (3 ml) containing DDQ (30 mg) was heated under reflux for 23 h in an atmosphere of nitrogen. After the removal of the solvent, the residue was dissolved in acetone and the solution was filtered through aluminum oxide. The removal of acetone gave a yellow product which was subjected to preparative TLC (Merck, silica gel 60 F_{254}) with a 1:1 hexane–ethyl acetate to give three fractions. The most mobile fraction (10 mg) was the starting material. The second mobile fraction was crystals of 11-oxaprogesterone (**15**) (2 mg, 11% based on the converted oxasteroid **14**) which was recrystallized from dichloromethane–diethyl ether. Mp 179—180 °C (lit,[2] 181—182 °C). ^{1}H NMR δ=0.80 (3H, s, 18-H), 1.26 (3H, s, 19-H), 2.07 (3H, s, 21-H), 2.59 (1H, J=9.98 Hz, 9α-H), 3.44 (1H, J=10.26 Hz, 12-H), 4.16 (1H, J=10.26 Hz, 12-H), and 5.78 (1H, s, 4-H). EIMS m/z 316 (M$^+$, 28), 193 (84), and 43 (100%).

The most polar fraction (6 mg, 31% based on the converted starting steroid) was 11-oxapregna-1,4-diene-3,20-dione which was recrystallized from dichloromethane–diethyl ether to give a pure specimen. Mp 193—196 °C (lit,[2] 195—196 °C), $[\alpha]_D^{22}$ +104.8° (c 0.8 in $CHCl_3$) [lit,[2] $[\alpha]_D^{22}$ +104.3° (c 1.0 in $CHCl_3$)]. ^{1}H NMR δ=0.83 (3H, s, 18-H), 1.32 (3H, s, 19-H), 2.07 (3H, s, 21-H), 2.63 (1H, d, J=9.52 Hz, 9α-H), 3.48 (1H, d, J=10.26 Hz, 12-H), 4.18 (1H, d, J=10.26 Hz, 12-H), 6.12 (1H, s, 4-H), 6.25 (1H, d, J=10.3 Hz, 2-H), and 7.26 (1H, s, J=10.3 Hz, 1-H), EIMS: m/z 314 (M$^+$, 16.5), 286 (5.8), 193 (42.3), and 42 (100%).

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