Photoinduced Molecular Transformations. 107.[1] A Versatile Substitution of a Carbonyl Group of Steroidal Ketones by a Heteroatom. The Synthesis of Aza-, Oxa-, Thia-, Selena-, and Tellurasteroids[2]

Hiroshi Suginome,* Shinji Yamada, and Jian Bo Wang

Organic Synthesis Division, Department of Chemical Process Engineering, Faculty of Engineering, Hokkaido University, Sapporo 060, Japan

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A new method is described for transforming steroidal six-membered cyclic ketones into steroidal cyclic amines, cyclic sulfides, cyclic tellurides, and cyclic selenides with the same ring size via five to six steps. Baeyer–Villiger oxidation of a steroidal ketone to the corresponding lactone followed by reduction with DIBAL gives the corresponding lactol. Irradiation of the hypoiodite, generated in situ by a reaction of the lactol with mercury(II) oxide–iodine in benzene, gives iodo formates arising from regiospecific β-scission. The transformation of these iodo formates into the corresponding diiodides with trimethylsilyl iodide followed by treatment of the resulting diiodides with either primary amines, sodium sulfide, or sodium telluride readily affords aza-, thia-, or tellurasteroids, respectively. Treatment of the diiodides with potassium selenocyanate, on the other hand, gives rise to monoselenocyanates, which can be readily converted into selenasteroids with sodium borohydride. The iodo formates can also by converted into cyclic sulfides through reductive hydrolysis with diisobutyl aluminum hydride (DIBAL) to iodo alcohols followed by mesylation and reaction of the resulting mesylates with sodium sulfide. 3-Thia-, 3-aza-, 3-tellura-, and 3-selena-5α-cholestanes, the corresponding 2,2,4,4-tetradeuterio derivatives, 6-thia-5β-cholestane, 11-thia-5β,9β-pregnan-3α-ol, and 16-thia-, 16-aza-, and 16-selena-5α-androstanes were thus synthesized from the corresponding steroidal ketones in fair to good yields. The synthesis of 11-oxa-5β-pregnan-3α-ol by our previously reported method is also described.

The replacement of one or more carbon atoms of a steroid molecule with heteroatoms brings about notable modifications of its biological activity; numerous studies exist[3] that deal with total and partial syntheses of heterosteroids as well as their physiological activities.

For example, Engel and colleagues[4] have found that replacement of the 11-carbon atom of pregnane skeleton resulted in interesting modifications of the biological activities.[5] Wolff and Zanati have reported that some A-ring heteroandrostanes have androgenic activity on the order of that of testosterone.[6] A-ring azasteroids have also been reported to inhibit the enzyme 5α-reductase in the conversion of testosterone to dihydrotestosterone.[7] Antibacterial[8] and neuromuscular-blocking activities[9] have also been found for some azasteroids.

In previous papers,[10-14] we have described the synthesis of several oxasteroids and cyclic ethers based on a new general method for substituting the hydroxymethine or carbonyl group of cyclic alcohols or cyclic ketones by an oxygen atom.

In this paper, we describe a further application of our method to the synthesis of an 11-oxasteroid, 3α-hydroxy-11-oxa-5β-pregnane, as well as its extension to a new, efficient synthesis of heterosteroids in which a carbon atom of the steroidal nucleus is replaced by a nitrogen, sulfur, selenium, or tellurium atom.

This method may be applicable not only to the synthesis of heterosteroids but also to the transformation of appropriate cyclic ketones into cyclic sulfides, cyclic amines, cyclic selenides, and cyclic tellurides, with the same ring size as the starting ketones. It may therefore complement or replace some of the earlier methods that have been used for synthesizing these classes of heterocycles, especially heterosteroids.

Results

Scheme I outlines our methods by which the five- and six-membered cyclic ketones are transformed into heterosteroids. Thus, cyclic ketones (A) are transformed into the corresponding lactols (C) by a Baeyer–Villiger oxidation followed by a reduction of the resulting lactones B with DIBAL. Irradiation of the lactols (C) in benzene in the presence of $HgO-I_2$ gives iodo formates (D), which are then transformed into oxasteroids (E) by treatment with sodium borohydride or methyllithium.[10-14] The iodo formates (D) are further transformed into the corresponding diiodides (F) by treatment with trimethylsilyl iodide,[15] in high yield. Treatment of the diiodides (F) with a primary

(1) Part 106: Suginome, H.; Satoh, G.; Wang, J. B.; Yamada, S.; Kobayashi, K. *J. Chem. Soc., Perkin. Trans. 1*, in press.

(2) Part of this work has been published as preliminary communications. (a) Suginome, H.; Yamada, S. *Chem. Lett.* **1984**, 2079. (b) Suginome, H.; Wang, J. B.; Yamada, S. *Ibid.* **1987**, 783.

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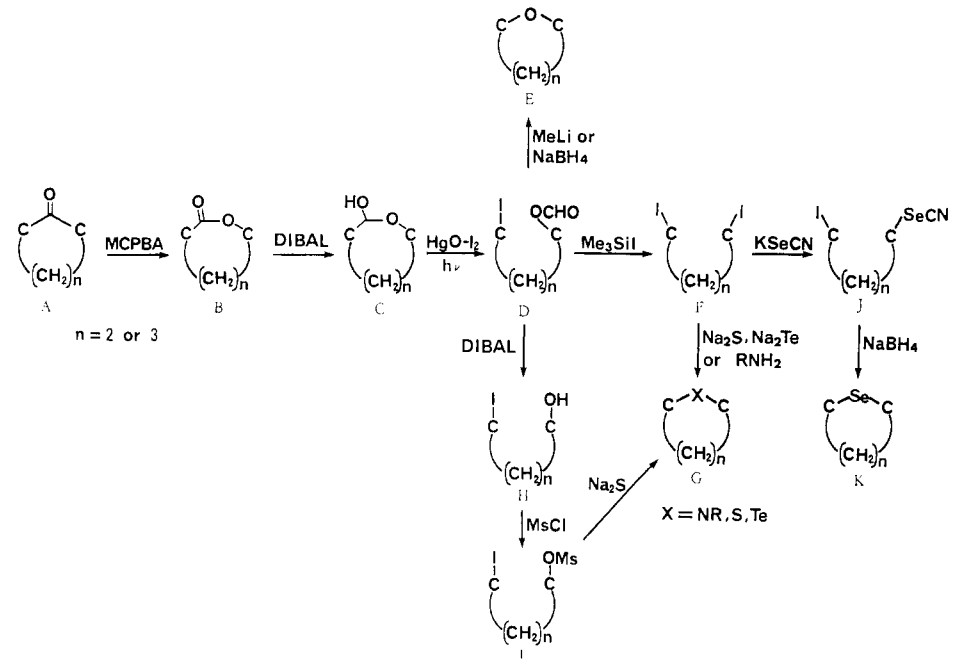
Scheme I



amine, sodium sulfide, or sodium telluride provides azasteroids (G, X = NR), thiasteroids (G, X = S), or telluraseroids (G, X = Te). Thus, a carbonyl group of the cyclic ketone is replaced by a nitrogen, sulfur, or tellurium atom in five steps. Although the cyclization of some diiodides (F) with sodium sulfide suffers from such disadvantages as the elimination of hydrogen iodide, we have nevertheless found that thiasteroids can be obtained in these cases through the following sequence of reactions: transformation of the iodo formates (D) with DIBAL into iodo alcohols (H), mesylation to the mesylates (I), and their cyclization to thiasteroids (G, X = S) by treatment with sodium sulfide.

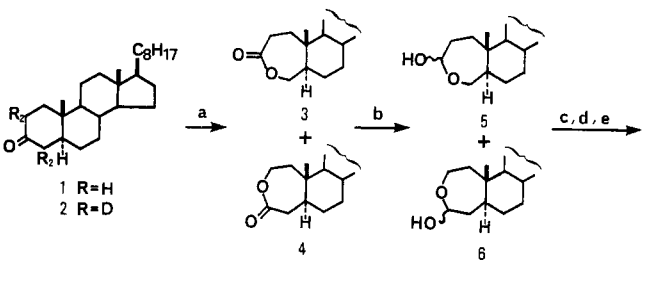
On the other hand, treatment of the diiodide (F) with 1 equiv of potassium selenocyanate in acetone gives rise to a monoselenocyanate (J), which can be converted readily into selenasteroids (K) with sodium borohydride. This method accomplishes the transformation of a steroidal ketone into selenasteroids with the same ring size in six steps.

We report here specific syntheses, based on the foregoing methods, of various ring-A, -B, -C, and -D heterosteroids.

Syntheses of 3-Thia-, 3-Aza-, 3-Tellura-, and 3-Selena-5α-cholestanes from 5α-Cholestan-3-one and of 2,2,4,4-Tetradeuterio Derivatives of 3-Oxa-, 3-Thia-, 3-Aza-, and 3-Selena-5α-cholestanes (Scheme II). 3-Thia-5α-cholestane (**12**) was synthesized by Dodson and colleagues[16] and subsequently by Mislow and colleagues.[17] Wolff and Zanati subsequently prepared 3-thia-, 3-selena-, 3-tellura-, and 3-oxa-*A*-nor-5α-androstanes.[6a,b] 3-Aza-5α-cholestane was prepared by Shoppee and colleagues.[18]

In the present study, a mixture of oily iodo formates **7** and **8**[11] obtained through lactones **3** and **4** and lactols **5** and **6** was treated with trimethylsilyl iodide[15] in carbon tetrachloride, to afford 2,3-diiodo-2,3-seco-*A*-nor-5α-cholestane (**9**) in 93% yield. Refluxing a solution of diiodide **9** in ethanol with sodium sulfide gave 3-thia-5α-cholestane

Scheme II[a]



7 R=I, R'=OCHO
8 R=OCHO, R'=I
9 R=R'=I
10 R=SeCN, R'=I
11 R=I, R'=SeCN

12 X=S, R=H
13 X=S, R=D
14 X=SO2, R=H
15 X=NCH2CH2CH3, R=H
16 X=NCH2Ph, R=H
17 X=NCH2Ph, R=D
18 X=NH, R=H
19 X=Te, R=H
20 X=Se, R=H
21 X=Se, R=D
22 X=O, R=D

[a] (a) MCPBA–*p*-toluenesulfonic acid (PTSA)–CH_2Cl_2; (b) DIBAL–toluene; (c) HgO–I_2–pyridine–benzene–*hν*; (d) Me_3SiI–CCl_4; (e) KSeCN–acetone; (f) $Na_2S·9H_2O$–EtOH; (g) H_2O_2–CH_3CO_2H; (h) $CH_3CH_2CH_2NH_2$–dioxane; (i) $C_6H_5CH_2NH_2$–dioxane; (j) PtO_2–H_2–CH_3CO_3H; (k) Na_2Te–EtOH; (l) $NaBH_4$–THF–MeOH; (m) MeLi–THF.

(**12**)[16,17] in 92% yield. Oxidation of thiasteroid **12** with hydrogen peroxide in acetic acid gave the corresponding sulfone (**14**) in 98% yield.

On the other hand, treatment of diiodide **9** in dioxane with either propylamine or benzylamine under reflux gave *N*-propyl-3-aza-5α-cholestane (**15**) or the corresponding *N*-benzyl derivative **16** in 52 and 97% yields, respectively. Removal of the benzyl group of *N*-benzyl azasteroid **16** by hydrogenolysis in the presence of PtO_2 readily gave 3-aza-5α-cholestane (**18**),[18] which was isolated as its crystalline hydrochloride in 82% yield.

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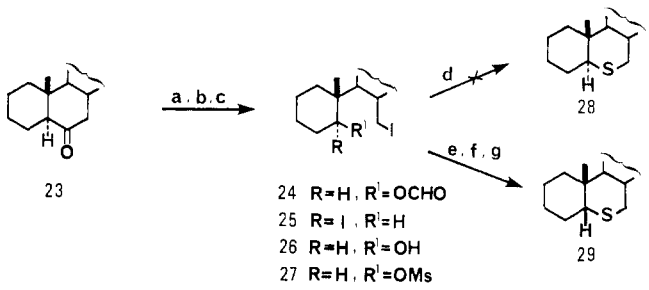
Scheme III[a]



[a] (a) MCPBA–PTSA–CH_2Cl_2; (b) DIBAL–hexane; (c) HgO–I_2–pyridine–benzene–$h\nu$; (d) Me_3SiI–CCl_4; (e) DIBAL–THF; (f) MsCl–pyridine; (g) $Na_2S{\cdot}9H_2O$–EtOH.

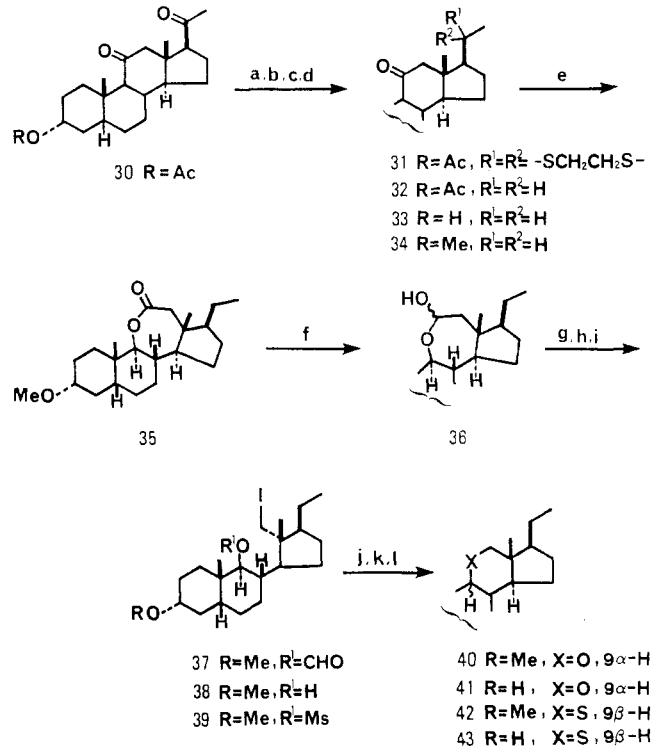
The diiodide **9** was similarly transformed into 3-tellura-5α-cholestane (**19**) by treatment with sodium telluride[19] in ethanol, in 34% yield. Upon treatment of the diiodide **9** with 1 equiv of potassium selenocyanate[20,21] in acetone gave a mixture of the monoselenocyanates **10** and **11**, which was converted in 78% yield to crystalline 3-selena-5α-cholestane (**20**) upon its slow addition to a solution of sodium borohydride in ethanol–tetrahydrofuran.[20,21] Heterosteroids **19** and **20** are the first 3-tellura- and 3-selenasteroids having a natural steroid skeleton.

The 2,2,4,4-tetradeuterio derivatives of the 3-oxa-, 3-thia-, 3-aza-, and 3-selena-5α-cholestanes, **22**, **13**, **17**, and **21**, were synthesized from 2,2,4,4-tetradeuterio-5α-cholestan-3-one (**2**)[22] in a similar manner.

Synthesis of 6-Thia-5β-cholestane from 5α-Cholestan-6-one (Scheme III). A stereoselective synthesis of 3β-hydroxy-6-thia-5α- and -5β-androstane and -cholestane has been reported by Speckamp and Kesselaar.[23] Jones and colleagues have converted cholesterol into 4-thia-5β-cholestane in nine steps.[24] An attempted transformation of 5α-cholestan-6-one (**23**) into 6-thia-5α-cholestane (**28**) by our preceding procedure proved to be unsuccessful; however, iodo formate **24**,[11] obtained in three steps from 5α-cholestan-6-one (**23**), was treated with trimethylsilyl iodide in carbon tetrachloride at 60 °C for 6 h, to give 5,6-diiodo-5,6-seco-*B*-nor-5β-cholestane (**25**); treatment of the diiodide **25** with sodium sulfide resulted only in the formation of 6-iodo-5,6-seco-*B*-norcholest-4-ene, which arose from the elimination of hydrogen iodide, and failed to give 6-thia-5α-cholestane. The synthesis of an isomeric 6-thia-5β-cholestane (**29**), however, could be achieved in three steps from the iodo formate (**24**): treatment of **24** with DIBAL in hexane at −78 °C gave 6-iodo-5,6-seco-*B*-nor-5α-cholestan-5-ol (**26**) in 90% yield. Its mesylation with mesyl chloride–pyridine to the corresponding mesyl ester **27** followed by treatment of the latter with sodium sulfide in ethanol gave 6-thia-5β-cholestane (**29**) in 40% yield (Scheme III).

Synthesis of 3α-Hydroxy-11-oxa-5β-pregnane (41) and 3α-Hydroxy-11-thia-5β,9β-pregnane (43) from 3α-Acetoxy-5β-pregnane-11,20-dione (30) (Scheme IV). The first synthesis of an 11-oxasteroid was achieved by Engel and colleagues in 12 steps from hecogenin by acid-catalyzed cyclization of a 9,11-seco-*C*-nor-5α-pregnane-9β,11-diol as the intermediate.[5,25,26] Bonet et al. have recently reported the transformation of estrone into 3-methoxy-11-oxaestrone by acid-catalyzed cyclization of 9,11-seco-*C*-nor-1,3,5(10)-estratriene-9β,11-diol obtained by dye-sensitized photooxygenation of a 1,3,5(10),9(11)-estratetraene.[27,28] The synthesis of 11-azasteroids has also been reported by Engel and colleagues[5,29] and subsequently by Badanova and Pivinitskic.[30]

Scheme IV[a]



[a] (a) BF_3–$HSCH_2CH_2SH$–Et_2O; (b) Raney Ni–dioxane; (c) KOH–EtOH–MeOH–H_2O; (d) MeI–NaH–THF; (e) MCPBA–H_2SO_4–CH_3CO_2H, H_2O_2–H_2SO_4–CH_3CO_2H, or $K_2S_2O_8$–H_2SO_4–CH_3CO_2H; (f) DIBAL–hexane; (g) HgO–I_2–benzene–$h\nu$; (h) DIBAL–toluene; (i) MsCl–pyridine; (j) $NaBH_4$–THF; (k) $Na_2S{\cdot}9H_2O$–CH_3CN; (l) Me_3SiI–$CHCl_3$.

We have found that our method can be applied to the synthesis of 11-oxasteroids as well as 11-thiasteroids from 11-oxosteroids.[2b] No report has so far been published on the synthesis of 11-thiasteroids, and the present synthesis of an 11-thiasteroid is, as far as we know, the first one to be achieved.

The 20-oxo group of commercially available 3α-acetoxy-5β-pregnane-11,20-dione (**30**) was removed by reduction of the thioketal group of the corresponding 20-thioketal derivative (**31**)[31] with Raney nickel, to give 3α-

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(26) Synthesis of 11-oxaestradiol and 11-oxa-1-dehydro-11-deoxycortisol has recently been reported after the submission of this paper. Engel C. R.; Ibrahim, I. H.; Mukherjee, D.; Szoghy, R.; Salvi, V. S. *Heterocycles* **1989**, *28*, 905.
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(28) A full account of this report has been published after the submission of this paper. Planas, A.; Sala, N.; Bonet, J. J. *Helv. Chim. Acta* **1989**, *72*, 725.
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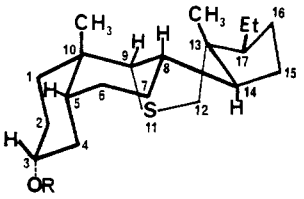


Figure 1.

acetoxy-5β-pregnan-11-one (32) in almost quantitative yield. Basic hydrolysis of acetate 32 gave the corresponding 3α-alcohol 33,[32] which was converted to 3α-methoxy-5β-pregnan-11-one (34) by treatment with methyl iodide–sodium hydride in THF, in over 95% yield.

To the best of our knowledge, no previous successful formation of lactones by means of Baeyer–Villiger oxidation of 11-oxosteroids has been reported; the Baeyer–Villiger oxidation of a steroidal 11,17-diketone, for example, has been reported to lead only to the formation of D-ring lactones.[33] Baeyer–Villiger oxidation of the 11-ketone 34 with *m*-chloroperbenzoic acid (MCPBA) in acetic acid containing concentrated sulfuric acid for 10 days resulted, however, in 34% conversion of the starting ketone and gave exclusively 3α-methoxy-11-oxa-*C*-homo-5α-pregnan-12-one (35) in 57% yield (based on the converted ketone). A similar oxidation of the 11-ketone with 35% hydrogen peroxide in acetic acid containing concentrated sulfuric acid for 10 days led to 36% conversion of the ketone to the lactone 35 in 61% yield. We then found that the oxidation of ketone 34 with potassium persulfate in glacial acetic acid–concentrated sulfuric acid (3:0.5 in volume) for 10 days at room temperature gave the best yield (62%) of lactone 35. No regio- or stereoisomers of lactone 35 were formed. Lactone 35 was then reduced with DIBAL to give a crystalline lactol 31 (98%), which was converted into the corresponding hypoiodite with a mercury(II) oxide–iodine reagent in benzene. Subsequently, the product was subjected in situ to the photolysis previously reported by us,[11] to give the crystalline iodo formate 37 in 83% yield. Ring-closure was effected with sodium borohydride in tetrahydrofuran under reflux, to give 3α-methoxy-11-oxa-5β-pregnane (40) in 93% yield. Finally, treatment of oxasteroid 40 with trimethylsilyl iodide in chloroform at room temperature for 12 h gave 3α-hydroxy-11-oxa-5β-pregnane (41) in 84% yield.

On the other hand, the formyloxy group of the iodo formate 37 was subjected to reductive hydrolysis with DIBAL in toluene at −78 °C, to give iodo alcohol 38 in 90% yield. Treatment of the latter with mesyl chloride under standard conditions gave the corresponding mesylate 39 in 71% yield. The first 11-thiasteroid, 3α-methoxy-11-thia-5β,9β-pregnane (42), was obtained in 33% yield by refluxing the acetonitrile solution of mesylate 39 and sodium sulfide. The yield of 11-thiasteroid 42 was not sufficiently high (33%), and ring-closure was accompanied by formation of a by product, which arose from an elimination reaction. Finally, treatment of thiasteroid 42 with trimethylsilyl iodide in chloroform for 12 h gave 3α-hydroxy-11-thia-5β,9β-pregnane (43) in 70% yield.

The 9α configuration assigned to oxasteroid 41 and the 9β configuration assigned to thiasteroid 43 were proved to be correct by their ^{1}H NMR spectra, which exhibited signals of their respective 9-protons at δ 3.12 with $J_{8\beta\text{-H}-9\alpha\text{-H}}$ = 9.89 Hz and at δ 2.49 with $J_{8\beta\text{-H}-9\beta\text{-H}}$ = 5.5 Hz.

Inspection of a model of thiasteroid 43 (with a 5β,9β configuration) indicates that rings A and C adopt the chair and boat conformations, respectively, while rings A and C are folded back under the B ring, as shown in Figure 1. This structure was further confirmed by the nuclear Overhauser enhancement: irradiation of the signal of the 19-proton of thiasteroid 43 resulted in an enhancement of the signal of the 9β-proton.

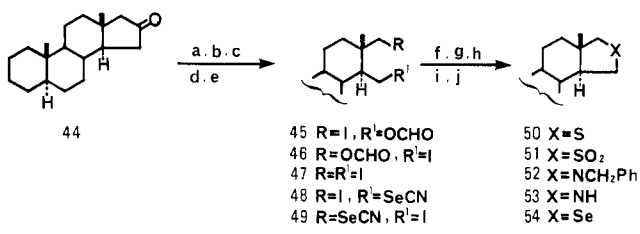
Since we published the preliminary results of the partial synthesis of 11-oxa- and 11-thiasteroids 41 and 43, we have achieved a new partial synthesis of 11-oxaprogesterone according to the method described in this paper. Details regarding this synthesis have been published elsewhere.[34]

Synthesis of 16-Thia-, 16-Aza-, and 16-Selena-5α-androstanes from 5α-Androstan-16-one (Scheme V). The transformation of steroidal 16-ones into 16-heterosteroids can be achieved in a similar fashion. A mixture of iodo formates 45 and 46[11] obtained from 5α-androstan-16-one (44) in three steps was treated with trimethylsilyl iodide in carbon tetrachloride at 60 °C for 48 h, to give 15,16-diiodo-15,16-seco-*D*-nor-5α-androstane (47) in 96% yield. Treatment of diiodide 47, either with sodium sulfide in ethanol or with benzylamine in dioxane, afforded 16-thia-5α-androstane (50) or *N*-benzyl-16-aza-5α-androstane (52) in 85 or 69% yield, respectively. Hydrogenolysis of *N*-benzyl-16-aza-5α-androstane (52) in acetic acid in the presence of Adams platinum oxide at room temperature for 2 days gave crystalline 16-aza-5α-androstane (53), which was very sensitive to air.

Oxidation of 16-thia-5α-androstane (50) in acetic acid with hydrogen peroxide (30%) at room temperature gave the corresponding sulfone 51 in excellent yield.

Diiodide 47, on the other hand, was dissolved in acetone containing potassium selenocyanate and heated under reflux for 3 h, to give an oily mixture of the isomeric monoselenocyanates 48 and 49 in 79% yield. This mixture, dissolved in tetrahydrofuran–ethanol, was treated with $NaBH_4$ at 40 °C for 70 h, to give crystalline 16-selena-5α-androstane (54).

Scheme V[a]



[a] (a) MCPBA–PTSA–CH_2Cl_2; (b) DIBAL–toluene; (c) HgO–I_2–pyridine–benzene; (d) Me_3SiI–CCl_4; (e) KSeCN–acetone; (f) $Na_2S\cdot 9H_2O$–EtOH; (g) H_2O_2–CH_3CO_2H; (h) $C_6H_5CH_2NH_2$–dioxane; (i) PtO_2–H_2–CH_3CO_2H; (j) $NaBH_4$–THF–EtOH.

Experimental Section

General Methods. Regarding the instruments used and the general procedure of the photolysis, see ref 10.

Preparation of 2,3-Diiodo-2,3-seco-*A*-nor-5α-cholestane (9). To a solution of a mixture of iodo formates 7 and 8[11] (360 mg, 0.68 mmol) in dry carbon tetrachloride (3 mL) was added iodotrimethylsilane (408 mg, 2.00 mmol) dropwise over a period of 5–10 min. After the solution had been stirred for 4 days at 60–70 °C, diethyl ether was added. The organic layer was washed with 5% aqueous sodium hydrogen carbonate, 5% aqueous sodium thiosulfate, and saturated brine successively and then dried over anhydrous sodium sulfate. Evaporation of the solvent in vacuo

(31) U.S. Patent 3132160 (1964); *Chem. Abstr.* **1964**, *61*, 4433h.
(32) U.S. Patent 3132160 (1964); *Chem. Abstr.* **1964**, *61*, 4434a.
(33) Wendler, N. L.; Taub, D.; Slates, H. L. *J. Am. Chem. Soc.* **1955**, *77*, 3559 Lardon, A.; Schmidlin, J.; Wettstein, A.; Reichstein, T. *Helv. Chim. Acta* **1957**, *40*, 662.
(34) Suginome, H.; Wang, J. B. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 193.

left a red oil, which was passed through a short silica gel column (hexane as eluent), to give virtually pure diiodide **9** (386 mg, 93%): mp 75–77 °C (acetone–methanol); IR 1202 cm^{-1}; ^1H NMR (200 MHz) δ 0.64 (3 H, s, 18-H), 0.73 (3 H, s, 19-H), 2.81 (1 H, t, J = 10.25 Hz, 3-H) 3.08 (2 H, t, J = 9.02 Hz, 2-H), 3.48 (1 H, dd, J = 10.25, 2.20 Hz, 3-H); MS, m/z 612 (M^+, 1) 485 [$(M - I)^+$, 25], 57 (100); high-resolution mass spectrum for $C_{26}H_{46}I_2$ calcd 612.1690, found 612.1716.

Synthesis of 3-Thia-5α-cholestane (12). To a solution of diiodide **9** (22 mg, 0.036 mmol) in ethanol (2 mL) was added sodium sulfide nonahydrate (150 mg). After the solution was heated under reflux for 5 h, it was extracted with diethyl ether, washed with water and saturated brine, and dried over anhydrous sodium sulfate. The usual workup gave crystalline, crude 3-thia-5α-cholestane, which was purified by preparative TLC with benzene–hexane (1:3), to yield pure 3-thia-5α-cholestane (13 mg, 92%): mp 98–99 °C (acetone–methanol) (lit.[17] mp 98.5–99.5 °C); ^1H NMR (200 MHz) δ 0.64 (3 H, s, 18-H), 0.82 (3 H, s, 19-H), 1.98–2.36 (2 H, m, 2-H), 2.66 (1 H, dd, J = 13.43, 12.97 Hz, 4-H), 2.90 (1 H, dt, J = 13.43, 2.44 Hz, 4-H); MS, m/z 390 (M^+, 100), 375 [$(M - Me)^+$, 48], 235 (57).

3-Thia-5α-cholestane 3,3-Dioxide (14). To 3-thia-5α-cholestane (**12**) (16 mg, 0.041 mmol) in glacial acetic acid (12 mL) was added hydrogen peroxide (30%, 0.6 mL) dropwise at 5 °C. The solution was set aside and stirred continuously for $2^1/_2$ days at room temperature; after the addition of water, the solution was extracted with dichloromethane. The orgaic layer was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave sulfone **14**, which was recrystallized from hexane–ethyl acetate (17 mg, 98%): mp 247–250 °C; IR (Nujol) 1338, 1299, 1149, 959, 851 cm^{-1}; ^1H NMR (270 MHz) δ 0.66 (3 H, s, 18-H), 0.93 (3 H, s, 19-H), 2.63–3.10 (4 H, m, $CH_2SO_2CH_2$); MS, m/z 422 (M^+, 68.6), 407 [$(M - Me)^+$, 32], 267 (100). Anal. Calcd for $C_{26}H_{46}SO_2$: C, 73.88; H, 10.97; S, 7.59. Found: C, 73.60; H, 10.98; S, 7.62.

***N*-Propyl-3-aza-5α-cholestane (15).** A solution of diiodide **9** (45 mg, 0.073 mmol) and propylamine (0.5 mL) in dioxane (0.5 mL) was placed in a sealed test tube and heated in an autoclave at 80 °C for 20 h. The dichloromethane extract was washed with water and brine. The solution was dried over anhydrous sodium sulfate, and the usual workup gave an oily product, which was purified by preparative TLC with benzene–diethyl ether (5:1). The product was recrystallized from acetone–methanol, to give 16 mg (52%) of azasteroid **15**: mp 91–92 °C; IR (Nujol) 1162, 1129, 1113, 1071, 994, 860 cm^{-1}; ^1H NMR (200 MHz) δ 0.65 (3 H, s, 18-H), 0.79 (3 H, s, 19-H), 2.05–2.82 (4 H, m, 2-H and 4-H); MS, m/z 415 (M^+, 2), 386 [$(M - CH_2CH_3)^+$, 100]. Anal. Calcd for $C_{29}H_{53}N$: C, 83.78; H, 12.85; N, 3.37. Found: C, 83.77; H, 12.75; N, 3.54.

***N*-Benzyl-3-aza-5α-cholestane (16).** To a solution of diiodide **9** (150 mg, 0.25 mmol) in dioxane (1.2 mL) was added benzylamine (0.7 ml). The solution was heated under reflux for 20 h and extracted with dichloromethane. The extract was washed with water and saturated brine and dried over anhydrous sodium sulfate. The usual workup gave an oily product, which was purified by preparative TLC with benzene–diethyl ether (5:1), to give azacholestane **16** (112 mg, 97%): mp 68–70 °C (acetone); IR (Nujol) 1159, 1070, 1028 cm^{-1}; ^1H NMR (200 MHz) δ 0.63 (3 H, s, 18-H), 0.79 (3 H, s, 19-H), 1.91–2.87 (4 H, m, 2-H and 4-H), 3.70 (2 H, s, CH_2Ph); MS, m/z 463 (M^+, 100), 91 ($-CHC_6H_5^+$, 63). Anal. Calcd for $C_{33}H_{53}N$: C, 85.46; H, 11.52; N, 3.02. Found: C, 85.36; H, 11.49; N, 2.84.

3-Aza-5α-cholestane (18). *N*-Benzyl-3-aza-5α-cholestane (**16**) (40 mg, 0.086 mmol) was dissolved in glacial acetic acid (3 mL) containing platinum oxide (15 mg). The solution was stirred in an atmosphere of hydrogen for 2 days at room temperature. After removal of the catalyst, water was added and the product was extracted with dichloromethane. The solution was dried over anhydrous sodium sulfate. The usual workup gave crystalline, unstable 3-aza-5α-cholestane (**18**): IR (Nujol) 3400 (NH), 1276, 1158, 1123 cm^{-1}; ^1H NMR (200 MHz) δ 0.64 (3 H, s, 18-H), 0.78 (3 H, s, 19-H); MS, m/z 373 (M^+). This azasteroid was rapidly converted to the carbonate. It was therefore converted to its hydrochloride by treatment of its acetone solution with 2 N hydrochloric acid. The hydrochloride (29 mg, 82%) melted at 260–265 °C (lit.[18] mp 280–285 °C).

Synthesis of 3-Tellura-5α-cholestane (19). A mixture of powdered tellurium (130 mg, 1.02 mmol), Rongalite (340 mg), and aqueous sodium hydroxide (70 mg in 1 mL of water) was stirred at 60 °C for 2 h under nitrogen, to produce sodium telluride. The wine-colored solution was evaporated to dryness under reduced pressure. To the pale-yellow residue was added a solution of diiodide **9** (100 mg, 0.16 mmol) in dry ethanol (2 mL); the mixture was then heated under reflux for 5 h. The reaction was quenched by the addition of a 10% ammonium sulfate solution, and the organic layer was extracted with diethyl ether. The ethereal extract was washed with water, dried over anhydrous sodium sulfate, and evaporated, to give crude tellurasteroid **19**. Recrystallization from acetone–methanol yielded pure 3-tellura-5α-cholestane (**19**) (27 mg, 34%): mp 126–128 °C; ^1H NMR (200 MHz) δ 0.65 (3 H, s, 18-H), 0.74 (3 H, s, 19-H), 2.93–3.32 (2 H, m, CH_2Te); MS, m/z 488 (100), 486 (92), 484 (60), 483 (25), 482 (15), 329 (25), 95 (90); high-resolution mass spectrum for $C_{26}H_{46}Te$ calcd 488.2668, found 488.2642.

Monoselenocyanates 10 and 11 from Diiodide 9. Diiodide **9** (145 mg, 0.24 mmol) and potassium selenocyanate (35 mg, 0.24 mmol) in acetone (15 mL) were heated under reflux for 2 h. The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane. The solution was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a product, which was subjected to preparative TLC with hexane–benzene (4:1), to give two fractions. The more mobile fraction (100 mg, 69%) was the starting material, and the less mobile one (23 mg, 16%) was a mixture of oily monoselenocyanates **10** and **11**: IR (neat) 2150 (C≡N), 1383, 1217 cm^{-1}; MS, m/z 591 (M^+, 6.9), 464 [$(M - I)^+$, 27.6], 55 (100); high-resolution mass spectrum for $C_{27}H_{46}NISe$ calcd 591.1842, found 591.1849.

3-Selena-5α-cholestane (20). To a solution of sodium borohydride (50 mg, 1.31 mmol) in THF–ethanol (20 mL) was added a solution of the above-mentioned mixture of monoselenocyanates, **10** and **11** (38 mg, 0.064 mmol), in THF–ethanol (20 mL) dropwise at 40 °C over a period of 2 h. The solution was stirred at 40 °C for 67 h. The solvent was evaporated under reduced pressure, and the product was dissolved in dichloromethane. The solution was washed with brine and with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave selenacholestane **20**, which, after being purified by preparative TLC (4:1 hexane–benzene), afforded pure selenasteroid **20** (22 mg, 78%): mp 94–95 °C (hexane); IR (Nujol) 1245, 940 cm^{-1}; ^1H NMR (270 MHz) δ 0.64 (3 H, s, 18-H), 0.79 (3 H, s, 19-H), 2.73–3.03 (2 H, m, CH_2Se); MS, m/z 438 (M^+, 100), 437 (19.9), 423 [$(M - Me)^+$, 9.5], 329 (44.0). Anal. Calcd for $C_{26}H_{46}Se$: C, 71.36; H, 10.60. Found: C, 71.24; H, 10.56.

Synthesis of 6-Iodo-5,6-seco-*B*-nor-5α-cholestan-5-ol (26). To a solution of iodo formate **24**[11] (65 mg, 0.12 mmol) in dry THF (5 mL) at −78 °C was added diisobutylaluminum hydride (DIBAL) (20% in hexane, Ventron) (0.15 mL) dropwise over the course of 10 min. The solution was stirred for 3 h at −78 °C and poured into iced water. After removal of the precipitates, the solution was washed with water and dried over anhydrous sodium sulfate. The usual workup gave a crude product, which was subjected to preparative TLC with benzene, to yield virtually pure iodo alcohol **26** (59 mg, 98%): oil; IR (neat) 3375, 1260, 1185, 1045 cm^{-1}; ^1H NMR (200 MHz) δ 0.71 (3 H, s, 18-H), 1.14 (3 H, s, 19-H), 3.39 (1 H, dd, J = 10.5, 2.20 Hz, 6-H), 3.47 (1 H, dd, J = 10.5, 1.5 Hz, 6-H), 3.77 (1 H, dd, J = 9.76, 3.91 Hz, 5α-H); MS, m/z 502 (M^+, 0.6), 484 [$(M - H_2O)^+$, 0.3], 374 [$(M - HI)^+$, 39], 219 (100), 95 (70); high-resolution mass spectrum for $C_{26}H_{43}IO_2$ calcd 502.2672, found 502.2704.

6-Iodo-5,6-seco-*B*-nor-5α-cholestan-5-ol Mesylate (27). To a solution of iodo alcohol **26** (58 mg, 0.11 mmol) in dry pyridine (2 mL) was added mesyl chloride (0.5 mL) dropwise in a nitrogen atmosphere at 0 °C. The solution was stirred for 10 h at 0 °C and worked up by the usual method, to yield an oily product, **27** (68 mg), which was used in the next step without further purification: IR (neat) 1179, 903 cm^{-1}.

6-Thia-5β-cholestane (29). To a solution of the iodo mesylate **27** (68 mg, 0.12 mmol) in ethanol (3 mL) was added sodium sulfide nonahydrate (400 mg). The solution was heated under reflux for 5 h and worked up, as described for the synthesis of **12**, to yield an oily product (50 mg). This was subjected to preparative TLC

with hexane, to give pure crystals of 6-thia-5β-cholestane (**29**) (18 mg, 40%): mp 94–95 °C (methanol); IR (Nujol) 1305, 1236, 952 cm^{-1}; ^1H NMR (200 MHz) δ 0.67 (3 H, s, 18-H), 1.19 (3 H, s, 19-H), 2.20 (1 H, br s, 5β-H), 2.27 (1 H, dd, J = 13.4, 3.4 Hz, 7α-H), 2.49 (1 H, dd, J = 13.4, 11.5 Hz, 7β-H); MS, m/z 390 (M^+, 9), 321 (100). Anal. Calcd for $C_{26}H_{46}S$: C, 79.92; H, 11.87; S, 8.21. Found: C, 79.99; H, 11.96; S, 7.98.

3α-Acetoxy-5β-pregnane-11,20-dione 20-Thioketal (31). This 20-thioketal was prepared from 3α-acetoxy-5β-pregnane-11,20-dione (**30**) by the standard method (boron trifluoride–ethanedithiol–diethyl ether, 0.5 h), 97%: mp 181–182 °C (lit.[31] mp 176–177 °C); IR (Nujol) 1736 (OAc), 1700 (C=O), 1242 cm^{-1}; ^1H NMR (270 MHz) δ 0.76 (3 H, s, 18-H), 1.15 (3 H, s, 19-H), 1.82 (3 H, s, 21-H), 2.02 (3 H, s, OAc), 3.16–3.40 (4 H, m, SCH_2CH_2S), 4.71 (1 H, m, 3β-H); MS, m/z 450 (M^+, 1.2), 435 [$(M - Me)^+$, 0.76], 390 [$(M - AcOH)^+$, 0.22], 119 (100). Anal. Calcd for $C_{25}H_{38}O_3S_2$: C, 66.62; H, 8.50; S, 14.23. Found: C, 66.50; H, 8.67; S, 14.18.

3α-Acetoxy-5β-pregnan-11-one (32). This was prepared from thioketal **31** (cf. above) by reduction with Raney Ni: mp 104–105 °C (methanol); IR (Nujol) 1730 (OAc), 1702 (C=O), 1455 cm^{-1}; ^1H NMR (270 MHz) δ 0.52 (3 H, s, 18-H), 0.87 (3 H, t, J = 7.33 Hz, 21-H), 1.17 (3 H, s, 19-H), 2.05 (3 H, s, OAc), 4.71 (1 H, m, 3β-H); MS, m/z 360 (M^+, 10.1), 300 [$(M - AcOH)^+$, 56.9], 285 (41.0), 205 (100); high-resolution mass spectrum for $C_{23}H_{36}O_3$ calcd 360.2664, found 360.2643.

3α-Hydroxy-5β-pregnan-11-one (33). This alcohol was prepared by hydrolysis of the above acetate **32** with methanolic potassium hydroxide: mp 158–161 °C (lit.[32] mp 153–154 °C); IR (Nujol) 3270 (OH), 1700 (C=O), 1456 cm^{-1}; ^1H NMR (270 MHz) δ 0.52 (3 H, s, 18-H), 0.87 (3 H, t, J = 7.33 Hz, 21-H), 1.16 (3 H, s, 19-H), 3.64 (1 H, m, 3β-H); MS, m/z 318 (M^+, 36.7), 300 [$(M - H_2O)^+$, 61.0], 285 (52.3), 246 (100). Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.24; H, 10.69. Found: C, 79.06; H, 10.74.

3α-Methoxy-5β-pregnan-11-one (34). To a solution of 3α-hydroxy-5β-pregnan-11-one (**33**) (8.1 g, 25.5 mmol) in dry THF was added sodium hydroxide (3.0 g) at 0 °C. The solution was stirred for 20 min, and methyl iodide (4.1 mL) was added. The solution was stirred at room temperature for about 10 h until the starting alcohol had nearly disappeared. The solvent was evaporated, and the residue was dissolved in dichloromethane. The usual workup gave oily 3β-methoxy-5β-pregnan-11-one (**34**) (8.0 g, 94%): IR (neat) 1700 (C=O), 1100 cm^{-1}; ^1H NMR (270 MHz) δ 0.51 (3 H, s, 18-H), 1.16 (3 H, s, 19-H), 3.14 (1 H, m, 3β-H), 3.34 (3 H, s, OMe); MS, m/z 332 (M^+, 42.9), 300 [$(M - MeOH)^+$, 74.9], 285 [$(M - MeOH - Me)^+$, 68.0], 246 (100); high-resolution mass spectrum for $C_{22}H_{36}O_2$ calcd 332.2714, found 332.2712.

Baeyer–Villiger Oxidation of 3α-Methoxy-5β-pregnan-11-one (34). (a) With MCPBA. To a solution of 3α-methoxy-5β-pregnan-11-one (**34**) (200 mg, 0.60 mmol) in acetic acid (5 mL) containing concentrated sulfuric acid (98%) was added MCPBA (640 mg). The solution was stirred for 10 days at room temperature in the absence of light. The solution was then diluted with water and extracted with dichloromethane. The organic layer was washed successively with a 5% $Na_2S_2O_3$ solution, saturated brine, and water and was dried over anhydrous magnesium sulfate. The oily product, obtained by evaporation of the solvent, was subjected to preparative TLC (2:1 hexane–ethyl acetate), to give two fractions. The more mobile fraction (133 mg, 66.5%) was the starting material, and the less mobile one (40 mg, 19%) was 3α-methoxy-11-oxa-*C*-homo-5β-pregnan-12-one (**35**): mp 127–129 °C (hexane); IR (Nujol) 1718 (lactone C=O), 1100 cm^{-1}; ^1H NMR (270 MHz) δ 0.67 (3 H, s, 18-H), 1.07 (3 H, s, 19-H), 2.43 (1 H, d, J = 13.9 Hz, 12α-H), 2.68 (1 H, d, J = 13.9 Hz, 12α-H), 3.20 (1 H, m, 3β-H), 3.36 (3 H, s, OMe), 4.29 (1 H, d, J = 9.5 Hz, 9α-H); MS, m/z 348 (M^+, 45.4). Anal. Calcd for $C_{22}H_{36}O_3$: C, 75.82; H, 10.41. Found: C, 75.83; H, 10.42.

(b) With Hydrogen Peroxide. To a solution of 3α-methoxy-5β-pregnan-11-one (**34**) (200 mg, 0.60 mmol) in acetic acid (5 mL) containing concentrated sulfuric acid (98%) was added hydrogen peroxide (35%, 0.8 mL). The solution was stirred for 10 days and worked up as described for the oxidation with MCPBA, to yield lactone **35** (45 mg, 21%) and the starting material (**34**) (128 mg, 64%).

(c) With Potassium Persulfate. To a solution of 3α-methoxy-5β-pregnan-11-one (**34**) (200 mg, 0.60 mmol) in glacial acetic acid (3 mL) were added potassium persulfate (1.00 g) and concentrated sulfuric acid (1 mL) in glacial acetic acid (3 mL). The mixture was stirred for 10 days at room temperature in the absence of light. The solution was worked up as usual, to give lactone **35** (56 mg, 27%) and the starting material (**34**) (113 mg, 56%).

Reduction of 3α-Methoxy-11-oxa-*C*-homo-5β-pregnan-12-one (35) with DIBAL. Reduction of lactone **35** (500 mg, 1.43 mmol) in dry toluene (30 mL) with DIBAL (1.0 M in hexane, 10 mL) from −78 °C to room temperature for 5 h (as described previously) gave a crude crystalline mixture of lactols **36** (497 mg, 99%), which was recrystallized from ethyl acetate–acetone, to give a mixture of the pure 3α-methoxy-11-oxa-*C*-homo-5β-pregnan-12-ols (**36**) (474 mg, 94%): mp 179.5–181 °C; IR (Nujol) 3450 (OH), 1020, 1005 cm^{-1}; ^1H NMR (270 MHz) δ 0.73 (3 H, s, 18-H), 0.93 (3 H, s, 19-H), 3.26 (1 H, m, 3β-H), 3.35 (3 H, s, OMe), 3.85 (1 H, d, J = 9.5 Hz, 9α-H), 5.16 (1 H, m, 12-H); MS, m/z 350 (M^+, 27.3), 332 (100). Anal. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.19; H, 10.99.

3α-Methoxy-11-oxa-5β-pregnane (40). To a solution of lactol **36** (100 mg, 0.28 mmol) in dry benzene (20 mL) were added mercury(II) oxide (187 mg, 0.84 mmol) and iodine (219 mg, 0.84 mmol). The solution was placed in a Pyrex vessel, flushed with nitrogen, and irradiated for 3 h with a 100-W high-pressure mercury arc (EIKOSHA). The solution was worked up in the usual manner, to give crystalline iodo formate **37** (113 m, 85%): mp 107.5–109 °C; IR (Nujol) 1701 cm^{-1} (OCHO); ^1H NMR (270 MHz) δ 0.80 (3 H, s, 18-H), 1.04 (3 H, s, 19-H), 3.35 (3 H, s, OMe), 3.24 (1 H, d, J = 10.26 Hz, 12-H), 3.29 (1 H, d, J = 10.26 Hz, 12-H), 5.12 (1 H, d, J = 11.4 Hz, 9α-H), 8.30 (1 H, d, J = 1.1 Hz, OCHO); MS, m/z 349 [$(M - I)^+$, 0.3], 303 [$(M - I - OCHOH)^+$, 18.3], 271 (100); high-resolution mass spectrum for $C_{22}H_{37}O_3$ $(M - I)^+$ calcd 349.2743, found 349.2720. Iodo formate **37** (84 mg, 0.18 mmol) and sodium borohydride (84 mg, 2.2 mmol) were dissolved in dry THF (5 mL). The solution was heated under reflux for 44 h. The usual workup gave oily 3α-methoxy-11-oxa-5β-pregnane (**40**) (54 mg, 93%): IR (neat), 1100, 1062, 1073 cm^{-1}; ^1H NMR (270 MHz) δ 0.72 (3 H, s, 18-H), 1.02 (3 H, s, 19-H), 3.09 (1 H, d, J = 9 Hz, 12-H), 3.13 (1 H, d, J = 9 Hz, 12-H), 3.35 (3 H, s, OMe), 3.86 (1 H, d, J = 10.3 Hz, 9α-H); MS, m/z 320 (M^+, 27), 288 [$(M - MeOH)^+$, 100]; high-resolution mass spectrum for $C_{22}H_{36}O_2$ calcd 320.2715, found 320.2721.

11-Oxa-5β-pregnan-3α-ol (41). To a solution of 3α-methoxy-11-oxa-5β-pregnane (**40**) (20 mg, 0.062 mmol) in chloroform (20 mL) was added trimethylsilyl iodide (0.05 mL). The solution was left overnight at room temperature; methanol was then added to decompose any excess trimethylsilyl iodide. The solution was worked up as usual, to give a crude product, which was subjected to preparative TLC with hexane–ethyl acetate (3:1), to give 11-oxa-5β-pregnan-3α-ol (**41**) (16 mg, 84%): mp 139–140 °C (hexane); IR (Nujol) 3270 (OH), 1080, 1049, 1027 cm^{-1}; ^1H NMR (270 MHz) δ 0.72 (3 H, s, 18-H), 1.02 (3 H, s, 19-H), 3.11 (1 H, d, J = 10.26 Hz, 12-H), 3.12 (1 H, d, J = 9.89 Hz, 9α-H), 3.64 (1 H, m, 3β-H), 3.88 (1 H, d, J = 10.26 Hz, 12-H; MS, m/z 306 (M^+, 91), 191 (100). Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.38; H, 11.14.

3α-Methoxy-11-thia-5β,9β-pregnane (42). To a solution of iodo formate **37** (270 mg, 0.57 mmol) in dry toluene (20 mL) was added DIBAL (1.0 M in hexane, 5 mL) at −78 °C under a nitrogen atmosphere. The solution was stirred for 30 min at −78 °C and for an additional 6 h at room temperature. The usual workup gave an oily product (263 mg), which was subjected to preparative TLC (hexane–ethyl acetate, 3:1), to give iodo alcohol **38** (228 mg, 90%): IR (neat) 3475 (OH), 1100 cm^{-1}; ^1H NMR (270 MHz) δ 0.81 (3 H, s, 18-H), 0.96 (3 H, s, 19-H), 3.34 (3 H, s, OMe), 3.57 (1 H, t, 9α-H). This alcohol was used in the next step without further purification.

To a solution of iodo alcohol **38** (220 mg, 0.49 mmol) in pyridine (18 mL) was added methanesulfonyl chloride (1.0 mL) at 0 °C under a nitrogen atmosphere. The solution was stirred for 20 h at room temperature; the solvent was then evaporated and the product extracted with diethyl ether. The ethereal solution was worked up in the usual manner, and the crude product was subjected to preparative TLC, to afford crystalline mesylate **39** (206 mg, 80%): mp 107–109 °C (hexane); IR 1335, 1170 cm^{-1}; ^1H NMR (270 MHz) δ 0.87 (3 H, s, OMe), 4.87 (1 H, d, J = 19.99 Hz, 9α-H), 3.27 (1 H, d, J = 10.63 Hz, 12-H), 3.32 (1 H, d, J = 10.63 Hz, 12-H), 3.19 (1 H, m, 3β-H); MS, m/z 339 [$(M - I)^+$, 0.2],

271 (100); high-resolution mass spectrum for $C_{21}H_{35}OI$ (M − $CH_3SO_2OH)^+$ calcd 430.1733, found 430.1712.

To a solution of mesylate **39** (100 mg, 0.19 mmol) in acetonitrile (15 mL) was added sodium sulfide nonahydrate (370 mg); the solution was then heated under reflux for 3 days. The solvent was evaporated and the product dissolved in diethyl ether. The usual workup gave an oily product (75 mg), which was subjected to preparative TLC, to give 3α-methoxy-11-thia-5β,9β-pregnane (**42**) (21 mg, 33%) as an oily, pure product: IR 1361, 1195 cm^{-1}; ^1H NMR (270 MHz) δ 0.84 (3 H, s, 18-H), 1.11 (3 H, s, 19-H), 2.35 (1 H, d, J = 12.46 Hz, 12-H), 2.47 (1 H, d, J = 5.49 Hz, 9β-H), 2.60 (1 H, d, J = 12.46 Hz, 12-H), 3.41 (1 H, s, OMe), 3.40 (1 H, m, 3β-H); MS, m/z 335 (M^+, 33), 304 [$(M - MeOH)^+$, 100], 289 [$(M - MeOH - Me)^+$, 12]; high-resolution mass spectrum for $C_{21}H_{36}SO$ calcd 336.2487, found 336.2503.

11-Thia-5β,9β-pregnan-3α-ol (43). A solution of 3α-methoxy-11-thia-5β,9β-pregnane (**42**) (40 mg, 0.12 mmol) in chloroform was treated with trimethylsilyl iodide (0.1 mL) as for demethylation of 3α-methoxy-11-oxa-5β-pregnane, to give crystalline 11-thia-5β,9β-pregnan-3α-ol (**43**) (27 mg, 70%): mp 178–180 °C (hexane); IR (Nujol) 1292, 953 cm^{-1}; ^1H NMR (270 MHz) δ 0.84 (3 H, s, 18-H), 1.04 (3 H, s, 19-H), 2.37 (1 H, d, J = 12.5 Hz, 12-H), 2.49 (1 H, d, J = 5.5 Hz, 9β-H), 2.62 (1 H, d, J = 12.5 Hz, 12-H), 4.05 (1 H, m, 3β-H); MS, m/z 322 (M^+, 88), 304 [$(M - H_2O)^+$, 100], 289 [$(M - H_2O - Me)^+$, 14.5]; high-resolution mass spectrum for $C_{20}H_{34}SO$ calcd 322.2320, found 322.2313.

15,16-Diiodo-15,16-seco-*D*-nor-5α-androstane (47). To a solution of iodo formates **45** and **46**[4] (85 mg, 0.20 mmol) in dry carbon tetrachloride (2 mL) was added iodotrimethylsilane (0.05 mL) dropwise over a period of 5–10 min under a nitrogen atmosphere. The solution was heated at 60–70 °C for 2 days and worked up in the usual way, to yield a crystalline diiodide (125 mg). This was subjected to preparative TLC with hexane–benzene (10:1), to yield pure diiodide **47** (98 mg, 96%): mp 95–104 °C; IR 1304, 1239, 1182, 960, 850 cm^{-1}; ^1H NMR (200 MHz) δ 0.78 (3 H, s, 19-H), 1.08 (3 H, s, 19-H), 3.15 (2 H, dd, J = 11.23, 2.93, 15-H), 3.27 (2 H, s, 16-H); MS, m/z 500 (M^+, 2), 373 [$(M - I)^+$, 73], 109 (100); high-resolution mass spectrum for $C_{18}H_{30}I_2$ calcd 500.0438, found 500.0473.

16-Thia-5α-androstane (50). To a solution of diiodide **47** (40 mg, 0.08 mmol) in ethanol (3 mL) was added sodium sulfide nonahydrate (200 mg). The solution was heated under reflux for 4 h and worked up in the usual manner, to yield an oily product (23 mg), which was purified by preparative TLC with hexane, to yield 16-thia-5α-androstane (**50**) (19 mg, 86%): mp 96–97 °C (methanol–acetone); IR (Nujol) 1226, 1163, 968, 950 cm^{-1}; ^1H NMR δ 0.78 (3 H, s, 19-H), 0.90 (3 H, s, 18-H), 2.25–3.00 (4 H, m, 15-H and 17-H); MS, m/z 278 (M^+, 100). Anal. Calcd for $C_{18}H_{30}S$: C, 77.63; H, 10.86; S, 11.51. Found: C, 77.51; H, 10.87; S, 11.03.

16-Thia-5α-androstane 16,16-Dioxide (51). To a solution of thiasteroid **50** (28 mg, 0.10 mmol) in glacial acetic acid (20 mL) was added hydrogen peroxide (30%, 1.0 mL) dropwise at 5 °C; the solution was stirred for 48 h. After the addition of chloroform, the solution was washed successively with 5% aqueous $Na_2S_2O_3$, 2 N sodium hydroxide solution, and water and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave sulfone **51** (36 mg) from hexane–ethyl acetate (30 mg, 97%): mp 147–149 °C; IR (Nujol) 1304, 1221, 1227, 793 cm^{-1}; ^1H NMR (270 MHz) δ 0.71 (3 H, s, 19-H), 1.20 (3 H, s, 18-H), 2.79–3.22 (4 H, m, CH_2SO_2); MS, m/z 310 (M^+, 75.3), 295 [$(M - Me)^+$, 34.5)], 253 (67.6), 95 (100); high-resolution mass spectrum for $C_{18}H_{30}SO_2$ calcd 310.1966, found 310.1985.

***N*-Benzyl-16-aza-5α-androstane (52).** A solution of diiodide **47** (35 mg, 0.07 mmol) and benzylamine (0.5 mL) in dioxane (0.5 mL) was heated under reflux for 16 h. The workup (as described for the synthesis of **11**) yielded an oily product, which was subjected to preparative TLC with benzene–diethyl ether (1:1), to yield pure material (17 mg, 71%): IR 1228, 1139, 1072 cm^{-1}; ^1H NMR δ 0.79 (3 H, s, 19-H), 0.91 (3 H, s, 18-H), 2.35–2.68 (4 H, m, 15-H and 17-H), 3.80 (2 H, s, CH_2Ph); MS, m/z 351 (M^+, 67), 133 (100), 91 ($C_6H_5CH_2^+$, 67); high-resolution mass spectrum for $C_{25}H_{37}N$ calcd 351.2937, found 351.2930.

16-Aza-5α-androstane (53). *N*-Benzyl-16-aza-5α-androstane (**52**) (30 mg, 0.085 mmol) in glacial acetic acid (2 mL) containing platinum oxide (15 mL) was shaken in an atmosphere of hydrogen for 2 days at room temperature. After removal of the catalyst, water was added. After the solution was extracted with dichloromethane, the organic layer was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a residue, which was purified by preparative TLC with hexane–ethyl acetate (1:4), to give the very unstable 16-azasteroid **53**, which was very labile for carbon dioxide[18] in the atmosphere and was rapidly transformed into the carbonate, mp 228–230 °C (23 mg). We failed to obtain either its pure hydrochloride or acetyl derivative.

Monoselenocyanates 48 and 49 from Diiodide 47. Diiodide **47** (100 mg, 0.2 mmol) and potassium selenocyanate (30 mg, 0.2 mmol) in acetone (15 mL) were heated under reflux for 3 h. After evaporation of the solvent, the product was dissolved in diethyl ether. The solution was washed with saturated brine and with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent left a residue, which was subjected to preparative TLC with hexane–ethyl acetate (4:1), to give two fractions. The more mobile one (18 mg, 18%) was the starting material. The less mobile fraction (75 mg, 78%) was an oily mixture of the two isomers of monoselenocyanates **48** and **49**: IR (neat) 2150 (C≡N), 1382, 1263 cm^{-1}; MS, m/z 479 (M^+, 0.26), 352 [$(M - I)^+$, 10.2], 326 [$(M - I - CN)^+$, 100]; high-resolution mass spectrum for $C_{19}H_{30}NSeI$ calcd 479.0638, found 479.0588.

16-Selena-5α-androstane (54). To a solution of a mixture of monoselenocyanates **48** and **49** (62 mg, 0.13 mmol) in THF–EtOH (40 mL), was slowly added sodium borohydride (100 mg, 2.63 mmol) in 9:1 THF–EtOH (40 mL). The solution was stirred for 70 h at 40 °C. After evaporation of the solution, the residue was dissolved in dichloromethane. The solution was then washed with saturated brine and with water and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was purified by preparative TLC with hexane, to give selenaandrostane **54** (43 mg). Recrystallization from hexane gave a pure specimen (40 mg, 95%): mp 84–85 °C (hexane); IR (Nujol) 1270, 1190, 1161, 962 cm^{-1}; ^1H NMR (270 MHz) δ 0.77 (3 H, s, 19-H), 0.88 (3 H, s, 18-H), 2.30–3.10 (4 H, m, CH_2SeCH_2); MS, m/z 326 (M^+ 100), 325 (12.5), 311 [$(M - Me)^+$, 9.06]. Anal. Calcd for $C_{18}H_{30}Se$: C, 66.44; H, 9.29. Found: C, 66.30; H, 9.56.

Registry No. **7**, 93789-82-3; **8**, 93789-81-2; **9**, 96034-24-1; **10**, 125303-43-7; **11**, 125303-44-8; **12**, 16666-70-9; **14**, 125303-45-9; **15**, 96034-26-3; **16**, 96034-25-2; **18**, 2952-64-9; **18**·HCl, 35459-51-9; **19**, 125303-47-1; **20**, 125303-47-1; **24**, 93789-71-0; **25**, 96034-30-9; **26**, 96034-32-1; **27**, 96034-33-2; **29**, 96093-89-9; **30**, 1610-52-2; **31**, 15807-43-9; **32**, 95671-73-1; **33**, 55146-30-0; **34**, 125329-11-5; **35**, 113360-35-3; **36** (isomer 1), 125409-24-7; **36** (isomer 2), 125409-25-8; **37**, 113360-37-5; **38**, 113360-40-0; **39**, 113360-41-1; **40**, 113360-38-6; **41**, 125303-48-2; **42**, 125409-26-9; **43**, 125409-27-0; **45**, 93789-84-5; **46**, 93789-88-9; **47**, 96034-27-4; **48**, 125303-49-3; **49**, 125303-50-6; **50**, 96034-28-5; **51**, 125329-12-6; **52**, 96034-29-6; **53**, 125472-05-1; **54**, 125329-13-7; propylamine, 107-10-8; benzylamine, 100-46-9; ethanedithiol, 540-63-6.