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Synthesis of 5α-Cholestan-6-one Derivatives with Some Substituents at the C-1, C-2, or C-3 Position

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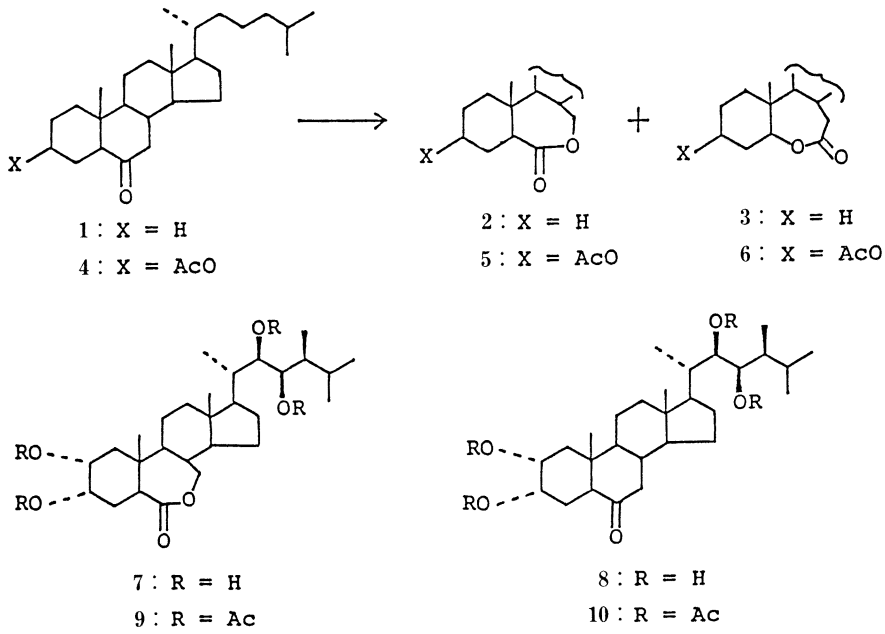
In order to investigate the regioselectivity of Baeyer–Villiger oxidation, thirty 5α-cholestan-6-one derivatives with various substituents (methyl, hydrogen, acetoxymethyl, methoxy, acetyloxy, benzoyloxy, trifluoroacetyloxy, *p*-toluenesulfonyloxy) at the C-1, C-2, or C-3 position were synthesized from cholesterol. The 6-oxo functional group of 5α-cholestan-6-one derivatives was introduced *via* hydroboration. The 3β-derivatives were readily obtained by using the native 3β-hydroxyl group of cholesterol. The 3α-isomers were obtained by inversion of the configuration of the 3β-tosylate **24** with tetra-*n*-butylammonium acetate in refluxing 2-butanone. The 2β-isomers were derived from the 2-ene **43** by bromohydrination, $LiAlH_4$ reduction, and esterification. The 2β- to 2α-hydroxyl group inversion was achieved by Birch reduction of the 2-oxo steroid **51**. The 1α-derivatives were derived from the known 6β-acetoxy-1α-hydroxy-5α-cholest-2-ene (**57**).

Keywords——Baeyer–Villiger oxidation; regioselectivity; 5α-cholestan-6-one derivative; hydroboration; configuration inversion; methoxymethyl group

In Baeyer–Villiger oxidation, the migratory aptitude of alkyl groups with retention of configuration is in the order of tertiary > secondary > primary, as expected from their relative abilities to stabilize an electron-deficient, tetrahedral transition state. It was reported that upon the oxidation of 5α-cholestan-6-one (**1**) with peracid, the 6-oxalactone **3** was obtained as a major product and its regioisomeric 7-oxalactone **2** as a minor product.[1] On the other hand, in the case of 3β-acetoxy-5α-cholestan-6-one (**4**) the major product was not the 6-oxalactone **6** but the 7-oxalactone **5**.[1] During the course of our synthesis of brassinolide (**7**) and castasterone (**8**), naturally occurring plant growth hormonal steroids, we also observed a similar unusual phenomenon in the Baeyer–Villiger oxidation of (22*R*,23*R*,24*S*)-2α,3α,22,23-tetraacetoxy-5α-ergostan-6-one (**10**); the C-7 carbon migrated more readily than the C-5 carbon, affording the 7-oxalactone **9** with *ca.* 90% regioselectivity.[2] This high regioselectivity, which can be ascribed to the effect of not only the 3α-acetoxyl but also the 2α-acetoxyl group, prompted us to investigate the regioselectivity of the Baeyer–Villiger oxidation of 5α-cholestan-6-one derivatives in more detail. We have prepared thirty 5α-cholestan-6-one derivatives with various substituents at the C-1, C-2, or C-3 position from cholesterol (**11**) and reported the regioselectivity of Baeyer–Villiger oxidation of them.[3] In this paper, we present details of the synthesis of the 5α-cholestan-6-one derivatives (**4**, **13**—**16**, **18**—**20**, **22**, **26**—**30**, **32**, **38**, **41**, **42**, **46**, **47**, **49**, **50**, **53**—**56**, **60**—**63**).

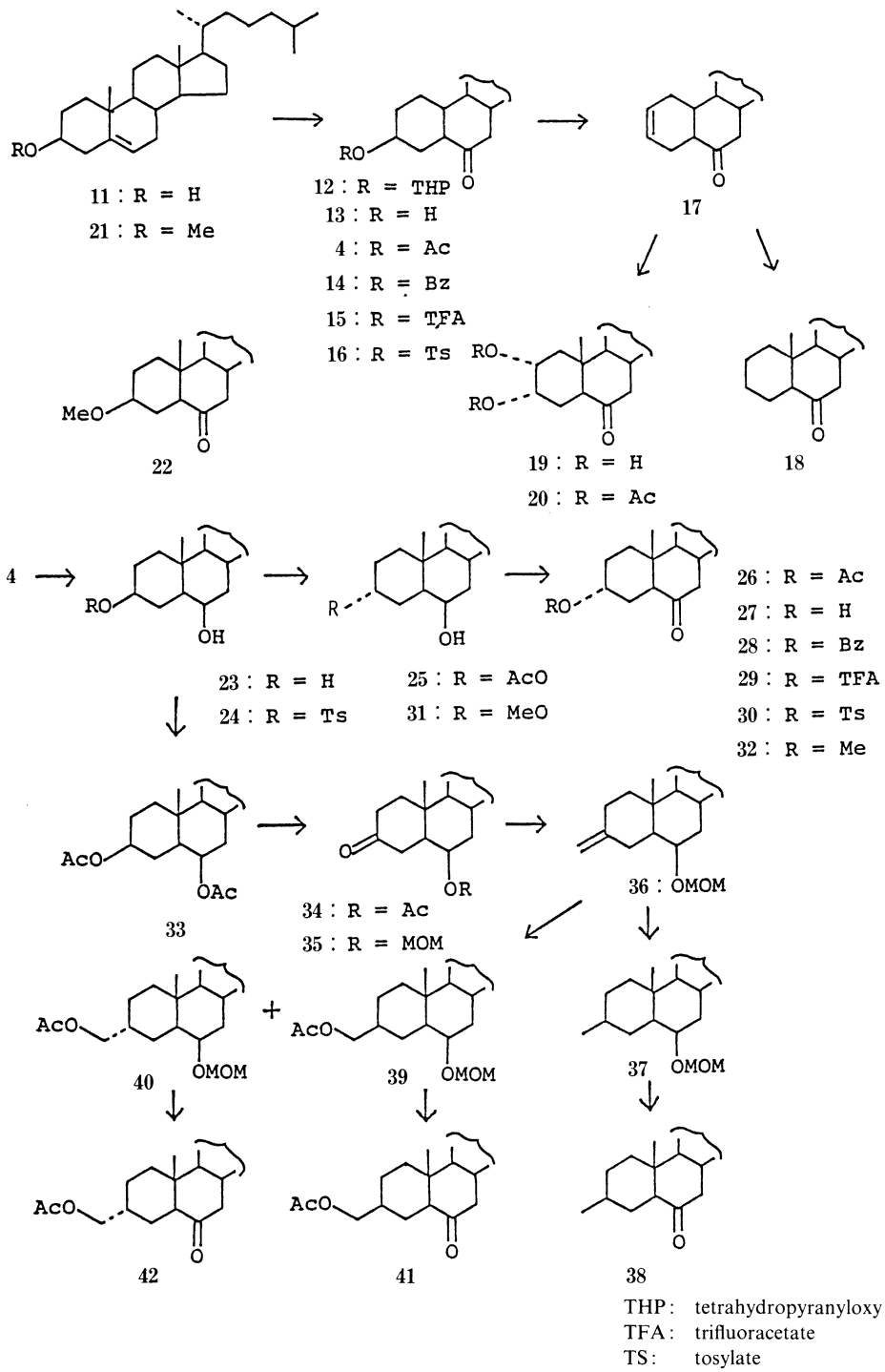
The 5α-cholestan-6-one derivatives (**4**, **13**—**16**) with substituents at the 3β-position were prepared from the known 3β-tetrahydropyranyloxy-5α-cholestan-6-one (**12**).[4] Acid hydrolysis of **12** gave 3β-hydroxy-5α-cholestan-6-one (**13**), which was converted into the corresponding acetate **4**, the benzoate **14**, the trifluoroacetate **15**, and the tosylate **16**. 3β-Methoxy-5α-cholestan-6-one (**22**) was synthesized from cholesterol methyl ether (**21**) as follows. Hydroboration of **21** with BH_3–tetrahydrofuran (THF) complex, followed by



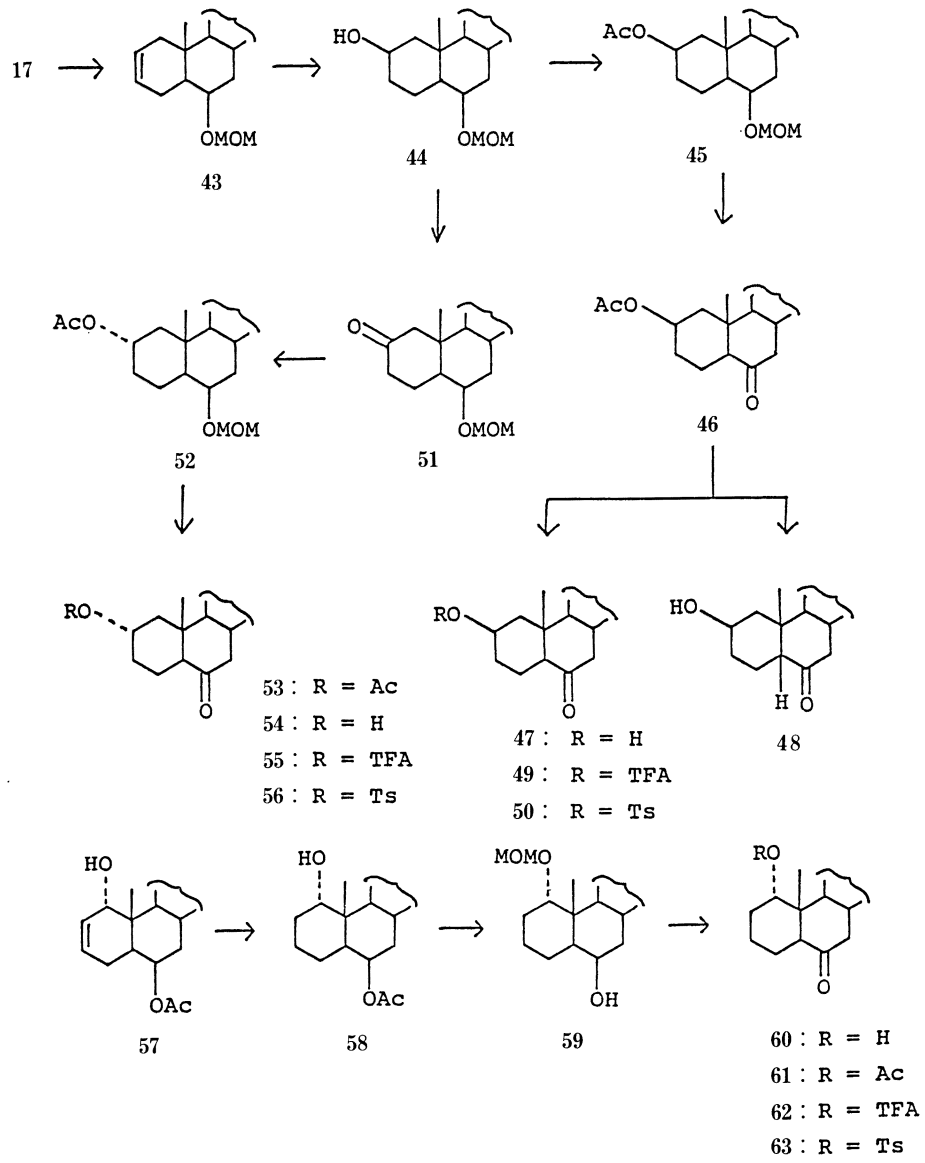
alkaline H_2O_2 oxidation gave 6α-hydroxy-3β-methoxy-5α-cholestane, which, without purification, was oxidized with Jones reagent. The 6-ketone **22** was obtained in 80% yield after chromatography.

The next target compounds were 5α-cholestan-6-one (**18**), 2α,3α-dihydroxy-5α-cholestan-6-one (**19**), and 2α,3α-diacetoxy-5α-cholestan-6-one (**20**). These 6-oxo steroids were prepared from the tosylate **16** according to our procedure used for the synthesis of brassinolide (**7**).[2] Thus, treatment of **16** with lithium bromide in refluxing dimethylformamide gave the 2-ene **17** in 95% yield. Hydrogenation provided 5α-cholestan-6-one (**18**), quantitatively. Stereoselective α-face hydroxylation of **17** was carried out with a catalytic amount of osmium tetroxide and an excess of *N*-methylmorpholine *N*-oxide in *tert*-BuOH–THF–H_2O (10 : 3 : 1) to afford the 2α,3α-diol **19**, which was then acetylated. The 2α,3α-diacetate **20** was obtained in 87% yield from **17**.

Next, we synthesized 5α-cholestan-6-one derivatives substituted at the 3α-position. Attempted inversion reaction of the 3β-tosylate **16** with various reagents (AcOK or AcONa/dimethylformamide (DMF) or dimethyl sulfoxide (DMSO), BzONa/DMF or DMSO, KO_2/18-crown-6/DMF–DMSO) and the Mitsunobu reaction of the 3β-ol **13** turned out to be fruitless because of the low yield of the inversion product. Therefore, we adopted the reported method,[5] which involves the inversion reaction of the 3β-tosyl-6β-ol **24** with tetra-*n*-butylammonium acetate. The substrate **24** was obtained as follows. Reduction of **13** with lithium aluminum hydride and recrystallization from ethyl acetate gave crystalline 3β,6β-dihydroxy-5α-cholestane (**23**) in 75% yield. Other stereoisomers were removed by recrystallization. Treatment of **23** with 1.14 eq of *p*-toluenesulfonyl chloride and pyridine gave the 3β-monotosylate **24** in 91% yield. Heating of **24** with tetra-*n*-butylammonium acetate and 2-butanone at reflux temperature gave the inversion product **25**, which was then oxidized with Jones reagent to afford 3α-acetoxy-5α-cholestan-6-one (**26**) in 50% yield. Saponification of **26** with 5% KOH/MeOH gave the 3α-ol **27**, which was converted into the benzoate **28**, the trifluoroacetate **29**, and the tosylate **30**. Refluxing of **24** with methanol also gave the inversion product **31**. Jones oxidation of **31** gave 3α-methoxy-5α-cholestan-6-one (**32**) in 50% yield.



The 3β-methyl, 3α- and 3β-acetoxymethyl derivatives **38**, **41**, **42** of 5α-cholestan-6-one were next synthesized. Acetylation of **23** gave the 3β,6β-diacetate **33**. Selective saponification of the 3β-acetyl group followed by Jones oxidation provided the known 6β-acetoxy-5α-



cholestan-3-one (**34**)[4] in 76% yield. After exchange of the acetyl group in **34** with a methoxymethyl (MOM) group, the 3-oxo compound **35** was submitted to Wittig reaction with methylenetriphenylphosphorane to give the olefin **36** in 73% yield from **34**. Hydrogenation of **36** provided the saturated compound **37** as a single product. The 3β-configuration was expected from the less hindered, α-face attack of hydrogen. Removal of the MOM group with conc. HCl was followed by Jones oxidation to give 3β-methyl-5α-cholestan-6-one (**38**) in 90% yield. Hydroboration of **36**, followed by alkaline H_2O_2 oxidation yielded, after acetylation, two separable products. Chromatographic separation gave the less polar 3α compound **40** and the more polar 3β compound **39**, in 50 and 27% yields, respectively. These were converted, as described for **38**, into the corresponding 3α-6-oxo steroid **42** (δ_H 4.04 (2H, d, $J=8$ Hz, $-C\underline{H}_2-OAc$)) and 3β-6-oxo steroid **41** (δ_H 3.90 (2H, d, $J=5$ Hz, $-C\underline{H}_2-OAc$)), respectively. The stereochemical assignment of **41** and **42** was based on the relative chemical shift due to the

acetoxy methylene in the proton nuclear magnetic resonance (^{1}H-NMR) spectra. The 3α-isomer should have lower chemical shift than the 3β-isomer because of the 1,3-diaxial interaction between the acetoxymethyl and 1α- and 5α-hydrogens.

Next we describe the synthesis of 5α-cholestan-6-one derivatives with C-2 substituents. Reduction of 5α-cholest-2-en-6-one (**17**) with lithium aluminum hydride was followed by protection of the resulting 6β-ol as the MOM ether to give **43**. Bromohydrination of **43** with *N*-bromosuccinimide/H_2O followed by reduction with lithium aluminum hydride provided the 2β-ol **44** (δ_H 4.10 (1H, m, $W_{1/2}=8$ Hz, 2α-H)) in 50% yield from **17**. The reaction possibly proceeded *via* the 2β,3β-epoxide, which suffered further reduction in *trans*-diaxial fashion. Acetylation of **44**, removal of the MOM group, and oxidation with pyridinium chlorochromate in the presence of sodium acetate gave 2β-acetoxy-5α-cholestan-6-one (**46**) in 79% yield. Saponification of **46** with 5% KOH/MeOH under reflux provided the less polar 5α compound **47** (19%, δ_H 4.15 (1H, m, $W_{1/2}=8$ Hz, 2α-H)) and the more polar 5β compound **48** (69%, δ_H 3.78 (1H, m, $W_{1/2}=24$ Hz, 2α-H)). 2β-Hydroxy-5α-cholestan-6-one (**47**) was converted into the trifluoroacetate **49** and the tosylate **50**.

The 2α-isomers **53**—**56** were prepared as follows. Jones oxidation of **44** gave the 2-oxo compound **51**. This was treated with Li/NH_3–EtOH and subsequently quenched with dry ammonium chloride to afford, after acetylation, the 2α-acetate **52** (δ_H 4.90 (1H, m, $W_{1/2}=$ 24 Hz, 2β-H)) as a single product in 86% yield from **44**. Regeneration of the 6-oxo functionality gave 2α-acetoxy-5α-cholestan-6-one (**53**) in 95% yield. 2α-Hydroxy-5α-cholestan-6-one (**54**), obtained by saponification of **53**, was converted into the trifluoroacetate **55** and the tosylate **56**.

The 6-oxo steroids with 1α-substituents were prepared from the known 6β-acetoxy-1α-hydroxy-5α-cholest-2-ene (**57**),[6] which was obtained from **34** according to the reported method.[6] Hydrogenation of **57** gave 6β-acetoxy-1α-hydroxy-5α-cholestane (**58**). Protection of the 1α-hydroxyl group of **58** as the MOM ether was followed by saponification to provide the 6β-ol **59**. This was submitted to Jones oxidation and then acid hydrolysis to afford 1α-hydroxy-5α-cholestan-6-one (**60**) in 80% overall yield. The alcohol **60** was converted into the acetate **61**, the trifluoroacetate **62**, and the tosylate **63**.

Experimental

Melting points were determined with a hot-stage microscope and are uncorrected. Infrared (IR) spectra were taken with a Hitachi 260-10 spectrometer in chloroform solution. ^{1}H-NMR spectra were taken with a Hitachi R-24A (60 MHz) or JEOL PS-100 (100 MHz) spectrometer in deuteriochloroform solution with tetramethylsilane as an internal standard. Column chromatography was done on Kieselgel 60 F_{254} (Merck, 70—230 mesh) and analytical thin layer chromatography (TLC) was carried out on precoated Kieselgel 60 F_{254} (Merck, 0.25 mm thickness). Work-up refers to dilution with water, extraction with the organic solvent indicated in parenthesis, washing of the extract to neutrality, drying over anhydrous magnesium sulfate, filtration, and removal of the solvent under reduced pressure. The following abbreviations are used; ether, diethyl ether; MeOH, methanol; EtOAc, ethyl acetate; $CHCl_3$, chloroform; CH_2Cl_2, dichloromethane.

3β-Hydroxy-5α-cholestan-6-one (13)——The crude 3β-tetrahydropyranyloxy-5α-cholestan-6-one (31 g) obtained from cholesterol (**11**) according to the reported method[4] was treated with 6 M HCl (50 ml) and THF (400 ml) at room temperature for 1 h. Work-up (ether) and chromatography on silica gel (150 g) with benzene–EtOAc (10 : 1) gave the 3β-ol **13** (22.4 g, 75% from **11**), mp 142—144 °C (MeOH). IR ν_{max} cm^{-1}: 1710. ^{1}H-NMR δ: 0.66 (3H, s, 18-H_3), 0.74 (3H, s, 19-H_3), 0.85 (6H, d, $J=6$ Hz, 26-H_3, 27-H_3), 3.54 (1H, m, 3-H). *Anal.* Calcd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.60; H, 11.54.

3β-Acetoxy-5α-cholestan-6-one (4)——The 3β-ol **13** (225 mg, 0.498 mmol) in pyridine (1 ml) was treated with acetic anhydride (1 ml) at room temperature overnight. Work-up (EtOAc) and chromatography on silica gel (20 g) with benzene gave the acetate **4** (182 mg, 82%), mp 129—130 °C (MeOH). ^{1}H-NMR δ: 0.67 (3H, s, 18-H_3), 0.80 (3H, s, 19-H_3), 0.85 (6H, d, $J=6$ Hz, 26-H_3, 27-H_3), 2.00 (3H, s, acetyl), 4.83 (1H, m, 3-H). *Anal.* Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.56; H, 10.85.

3β-Benzoyloxy-5α-cholestan-6-one (14)——The 3β-ol **13** (320 mg, 0.796 mmol) in pyridine (2 ml) was treated with benzoyl chloride (0.2 ml) at room temperature overnight. Work-up (EtOAc) and chromatography on silica gel (20 g)

with benzene gave the benzoate **14** (368 mg, 94%), mp 172—174 °C (MeOH). ^{1}H-NMR δ: 0.67 (3H, s, 18-H$_3$), 0.81 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 4.85 (1H, m, 3-H), 7.30—7.60 (3H, m, benzoyl), 7.90—8.10 (2H, m, benzoyl). *Anal.* Calcd for $C_{34}H_{50}O_3$: C, 80.58; H, 9.95. Found: C, 80.68; H, 9.93.

3β-Trifluoroacetoxy-5α-cholestan-6-one (15)——The 3β-ol **13** (402 mg, 1.0 mmol) in $CHCl_3$–pyridine (1 : 1, 2 ml) was treated with trifluoroacetic anhydride (0.3 ml) at room temperature overnight. Work-up (EtOAc) and chromatography on silica gel (20 g) with benzene gave the trifluoroacetate **15** (403 mg, 84%), mp 143—145 °C ($CHCl_3$–MeOH). ^{1}H-NMR δ: 0.66 (3H, s, 18-H$_3$), 0.79 (3H, s, 19-H$_3$), 0.86 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 4.86 (1H, m, 3-H). *Anal.* Calcd for $C_{29}H_{45}F_3O_3$: C, 69.85; H, 9.10. Found: C, 69.77; H, 8.98.

3β-*p*-Toluenesulfonyloxy-5α-cholestan-6-one (16)——The 3β-ol **13** (4.02 g, 10.0 mmol) in pyridine (30 ml) was treated with *p*-toluenesulfonyl chloride (3.8 g, 20.0 mmol) at room temperature overnight. Work-up (EtOAc) and chromatography on silica gel (100 g) with benzene gave the tosylate **16** (5.0 g, 90%), mp 175—177 °C (MeOH). ^{1}H-NMR δ: 0.63 (3H, s, 18-H$_3$), 0.71 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 0.90 (3H, d, J=6 Hz, 21-H$_3$), 2.45 (3H, s, tosyl), 4.50 (1H, m, 3-H), 7.40 (2H, d, J=8 Hz, tosyl), 7.90 (2H, d, J=8 Hz, tosyl). *Anal.* Calcd for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41. Found: C, 73.46; H, 9.50.

5α-Cholest-2-en-6-one (17)——The 3β-tosylate **16** (25 g, 45 mmol) in dimethylformamide (70 ml) was treated with anhydrous lithium bromide (10 g, 115 mmol) under reflux for 1 h. Work-up (EtOAc) and chromatography on silica gel (100 g) with benzene gave the 2-ene **17** (16.4 g, 95%), mp 97—98 °C (MeOH). IR ν_{max} cm^{-1}: 1710. ^{1}H-NMR δ: 0.65 (3H, s, 18-H$_3$), 0.67 (3H, s, 19-H$_3$), 0.84 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 5.53 (2H, m, 2-H, 3-H). *Anal.* Calcd for $C_{27}H_{44}O$: C, 84.31; H, 11.53. Found: C, 84.37; H, 11.33.

5α-Cholestan-6-one (18)——The 2-ene **17** (300 mg, 0.781 mmol) in EtOAc (20 ml) was treated with 5% Pd–C (30 mg) under a hydrogen atmosphere at room temperature overnight. Filtration and removal of the solvent gave 5α-cholestan-6-one (**18**) (300 mg), mp 97—98 °C (MeOH). ^{1}H-NMR δ: 0.66 (3H, s, 18-H$_3$), 0.72 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$).

2α,3α-Dihydroxy-5α-cholestan-6-one (19)——The 2-ene **17** (1.0 g, 2.6 mmol) in *tert*-BuOH–THF–H_2O (10 : 3 : 1, 10 ml) was treated with osmium tetroxide (20 mg) and *N*-methylmorpholine *N*-oxide (750 mg, 6.4 mmol) at room temperature overnight. Work-up (CH_2Cl_2) and chromatography on silica gel (30 g) with benzene–EtOAc (1 : 2) gave the 2α,3α-diol **19** (0.97 g, 89%), mp 206—207 °C ($CHCl_3$–MeOH).

2α,3α-Diacetoxy-5α-cholestan-6-one (20)——The 2α,3α-diol **19** (400 mg, 0.957 mmol) in pyridine (5 ml) was treated with acetic anhydride (4 ml) at 60 °C overnight. Work-up (EtOAc) and chromatography on silica gel (30 g) with benzene–EtOAc (25 : 1) gave the diacetate **20** (470 mg, 98%), mp 152—153 °C (MeOH). ^{1}H-NMR δ: 0.68 (3H, s, 18-H$_3$), 0.84 (3H, s, 19-H$_3$), 0.88 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 0.92 (3H, d, J=6 Hz, 21-H$_3$), 1.99 (3H, s, acetyl), 2.08 (3H, s, acetyl), 2.56 (1H, dd, J=9, 6 Hz, 5α-H), 4.92 (1H, m, $W_{1/2}$=22 Hz, 2β-H), 5.36 (1H, m, $W_{1/2}$=7 Hz, 3β-H). *Anal.* Calcd for $C_{31}H_{50}O_5$: C, 74.06; H, 10.02. Found: C, 74.03; H, 9.94.

3β-Methoxy-5α-cholestan-6-one (22)——Cholesterol methyl ether (**21**) (500 mg, 1.25 mmol) in THF (7 ml) was treated with 1 M BH_3–THF complex solution (3 ml) at room temperature for 6 h. Then, the reaction mixture was treated with 3 M NaOH (0.5 ml) and 30% H_2O_2 (0.5 ml) at room temperature for 1 h. Work-up (ether) gave a crude product. This in acetone (5 ml) was treated with 2 eq of Jones reagent at room temperature for 15 min. Work-up (ether) and chromatography on silica gel (20 g) with benzene gave the 6-oxo compound **22** (415 mg, 80%), mp 132—135 °C (MeOH–ether). ^{1}H-NMR δ: 0.66 (3H, s, 18-H$_3$), 0.75 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 3.00 (1H, m, 3-H), 3.36 (1H, s, –OCH$_3$). *Anal.* Calcd for $C_{28}H_{48}O_2$: C, 81.25; H, 11.29. Found: C, 81.18; H, 11.33.

6β-Hydroxy-3β-*p*-toluenesulfonyloxy-5α-cholestane (24)——3β-Acetoxy-5α-cholestan-6-one (**4**) (10 g, 22.5 mmol) in THF (50 ml) was treated with lithium aluminum hydride (2.0 g, 52.6 mmol) at room temperature for 1 h. Water was carefully added to decompose the excess hydride. Filtration and removal of the solvent gave a crude product, which was recrystallized from EtOAc to afford the 3β,6β-diol **23** (6.7 g, 75%), mp 189—190 °C. The diol **23** (6.5 g, 16.1 mmol) in pyridine (20 ml) was treated with *p*-toluenesulfonyl chloride (3.5 g, 18.4 mmol) at room temperature overnight. Work-up (ether) and chromatography on silica gel (70 g) with benzene gave the 3β-monotosylate **24** (7.96 g, 91%), mp 139—140 °C (hexane–EtOAc). ^{1}H-NMR δ: 0.66 (3H, s, 18-H$_3$), 0.90 (3H, s, 19-H$_3$), 2.41 (3H, s, tosyl), 3.72 (1H, m, $W_{1/2}$=8 Hz, 6α-H), 4.50 (1H, m, 3-H), 7.30 (2H, d, J=8 Hz, tosyl), 7.78 (2H, d, J=8 Hz, tosyl). *Anal.* Calcd for $C_{34}H_{54}O_4S$: C, 73.07; H, 9.74. Found: C, 73.15; H, 9.44.

3α-Acetoxy-5α-cholestan-6-one (26)——The tosylate **24** (6.7 g, 12.3 mmol) in 2-butanone (120 ml) was treated with tetra-*n*-butylammonium acetate (13 g, 43.2 mmol) under reflux for 20 h. Work-up (ether) and chromatography on silica gel (100 g) with benzene–EtOAc (100 : 1) gave the 3α-acetate **25** (3.13 g, 57%), mp 144—146 °C (MeOH) (lit.[5] mp 135—136 °C). ^{1}H-NMR δ: 0.69 (3H, s, 18-H$_3$), 0.86 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 0.90 (3H, d, J=6 Hz, 21-H$_3$), 1.01 (3H, s, 19-H$_3$), 2.03 (3H, s, acetyl), 3.71 (1H, m, $W_{1/2}$=7 Hz, 6α-H), 5.08 (1H, m, $W_{1/2}$=7 Hz, 3β-H). This product **25** (3.2 g, 7.17 mmol) in acetone (100 ml) was treated with 1 eq of Jones reagent at room temperature for 10 min. Work-up (ether) gave the 6-oxo steroid **26** (3.1 g), mp 106.5—107.5 °C (ether–MeOH) (lit.[5] mp 107—108 °C). ^{1}H-NMR δ: 0.68 (3H, s, 18-H$_3$), 0.75 (3H, s, 19-H$_3$), 0.86 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 0.90 (3H, d, J=6 Hz, 21-H$_3$), 2.04 (3H, s, acetyl), 2.54 (1H, dd, J=11, 5 Hz, 5α-H), 5.09 (1H, m, $W_{1/2}$=7 Hz, 3β-H). *Anal.* Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.52; H, 10.95.

3α-Hydroxy-5α-cholestan-6-one (27)——The acetate **26** (2.34 g, 5.04 mmol) in MeOH (50 ml) was treated with

5% KOH/MeOH (20 ml) at room temperature for 3 h. Work-up (ether) and chromatography on silica gel (30 g) with benzene–EtOAc (50 : 1) gave the 3α-ol **27** (1.5 g, 72%), mp 158—160 °C (ether–MeOH) (lit.[5] mp 160 °C). IR ν_{max} cm^{-1}: 1712. ^{1}H-NMR δ: 0.64 (3H, s, 18-H$_3$), 0.71 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 0.89 (3H, d, J=6 Hz, 21-H$_3$), 4.12 (1H, m, $W_{1/2}$=8 Hz, 3β-H).

3α-Benzoyloxy-5α-cholestan-6-one (28)——The 3α-ol **27** (300 mg, 0.746 mmol) was converted, as described for **14**, into the benzoate **28** (374 mg, 98%), mp 137—138 °C (ether–MeOH). ^{1}H-NMR δ: 0.66 (3H, s, 18-H$_3$), 0.79 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 2.67 (1H, dd, J=11, 5 Hz, 5α-H), 5.36 (1H, m, $W_{1/2}$=8 Hz, 3β-H), 7.30—7.60 (3H, m, benzoyl), 7.90—8.10 (2H, m, benzoyl). *Anal.* Calcd for $C_{34}H_{50}O_3$: C, 80.58; H, 9.95. Found: C, 80.57; H, 9.92.

3α-Trifluoroacetoxy-5α-cholestan-6-one (29)——The 3α-ol **27** (300 mg, 0.746 mmol) was converted, as described for **15**, into the trifluoroacetate **29** (324 mg, 87%), mp 105—106 °C ($CHCl_3$–MeOH). ^{1}H-NMR δ: 0.68 (3H, s, 18-H$_3$), 0.78 (3H, s, 19-H$_3$), 0.84 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 2.54 (1H, dd, J=10, 6 Hz, 5α-H), 5.33 (1H, m, $W_{1/2}$=8 Hz, 3β-H). *Anal.* Calcd for $C_{29}H_{45}F_3O_3$: C, 69.85; H, 9.10. Found: C, 70.10; H, 8.87.

3α-*p*-Toluenesulfonyloxy-5α-cholestan-6-one (30)——The 3α-ol **27** (193 mg, 0.48 mmol) was converted, as described for **16**, into the tosylate **30** (253 mg, 95%), mp 146—147 °C (ether–MeOH). ^{1}H-NMR δ: 0.62 (3H, s, 18-H$_3$), 0.65 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 2.39 (3H, s, tosyl), 2.54 (1H, dd, J=12, 5 Hz, 5α-H), 4.74 (1H, m, $W_{1/2}$=8 Hz, 3β-H), 7.28 (2H, d, J=8 Hz, tosyl), 7.72 (2H, d, J=8 Hz, tosyl). *Anal.* Calcd for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41. Found: C, 73.40; H, 9.23.

3α-Methoxy-5α-cholestan-6-one (32)——The mixture of the tosylate **24** (1.0 g, 1.79 mmol) and MeOH (50 ml) was refluxed for 2 d. Work-up (ether) and chromatography on silica gel (20 g) with benzene–EtOAc (20 : 1) gave the 3α-methoxy-6β-ol **31** (390 mg, 54%), oil. ^{1}H-NMR δ: 0.68 (3H, s, 18-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 1.00 (3H, s, 19-H$_3$), 3.29 (3H, s, –OCH$_3$), 3.55 (1H, m, $W_{1/2}$=8 Hz, 3β-H), 3.73 (1H, m, $W_{1/2}$=7 Hz, 6α-H). This in acetone (10 ml) was oxidized with Jones reagent to give the 6-oxo compound **32** (380 mg), mp 107—108.5 °C (MeOH). ^{1}H-NMR δ: 0.65 (3H, s, 18-H$_3$), 0.73 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 3.29 (3H, s, –OCH$_3$), 3.53 (1H, m, $W_{1/2}$=8 Hz, 3β-H). *Anal.* Calcd for $C_{28}H_{48}O_2$: C, 81.25; H, 11.29. Found: C, 80.87; H, 11.41.

3β,6β-Diacetoxy-5α-cholestane (33)——The 3β,6β-diol **23** (9.0 g, 22.28 mmol) in pyridine (100 ml) was treated with acetic anhydride (50 ml) at room temperature for 40 h. Work-up (EtOAc) and chromatography on silica gel (100 g) with benzene gave the diacetate **33** (9.86 g, 91%), mp 137—138 °C (MeOH). ^{1}H-NMR δ: 0.68 (3H, s, 18-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 0.90 (3H, d, J=6 Hz, 21-H$_3$), 1.00 (3H, s, 19-H$_3$), 2.01 (3H, s, acetyl), 2.03 (3H, s, acetyl), 4.75 (1H, m, 3-H), 4.95 (1H, m, 6-H).

6β-Acetoxy-5α-cholestan-3-one (34)——The diacetate **33** (8.56 g, 17.5 mmol) in THF–MeOH (1 : 2, 150 ml) was treated with 5% KOH/MeOH (40 ml) at room temperature for 45 min. Work-up (ether) gave a crude product, which was dissolved in acetone (200 ml). Then, Jones reagent (1 eq) was added and stirring was continued for 10 min. Work-up (ether) and chromatography on silica gel (100 g) with benzene–EtOAc (50 : 1) gave the 3-oxo steroid **34** (6.5 g, 83%), mp 97—99 °C (MeOH) (lit.[5] mp 99—102 °C). ^{1}H-NMR δ: 0.70 (3H, s, 18-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$), 0.90 (3H, d, J=6 Hz, 21-H$_3$), 1.14 (3H, s, 19-H$_3$), 2.02 (3H, s, acetyl), 4.85 (1H, m, 6-H). *Anal.* Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.19; H, 10.88.

6β-Methoxymethoxy-3-methylene-5α-cholestane (36)——The 6β-acetate **34** (3.0 g, 6.76 mmol) in dioxane (10 ml) was treated with 5% KOH/MeOH (30 ml) at 70 °C for 17 h. Work-up (ether) gave a crude product (2.8 g). This in dioxane (20 ml) was treated with chloromethyl methyl ether (4 ml) and diethylcyclohexylamine (5 ml) at room temperature for 4 h. Work-up (EtOAc) and chromatography on silica gel (50 g) with benzene–EtOAc (20 : 1) gave the methoxymethyl ether **35** (2.33 g, 76%).

A solution of *n*-butyl lithium in hexane (5.7 ml, 8.89 mmol) was added to a solution of methyltriphenylphosphonium iodide (2.5 g, 6.19 mmol) in THF (10 ml) at 0 °C. The mixture was stirred at room temperature for 10 min. Then, a solution of the ketone **35** (2.3 g, 5.16 mmol) in THF (10 ml) was added to the ylide solution. The mixture was stirred at room temperature for 1 h. Work-up (EtOAc) and chromatography on silica gel (30 g) with benzene–EtOAc (50 : 1) gave the olefin **36** (2.2 g, 96%), oil. ^{1}H-NMR δ: 0.69 (3H, s, 18-H$_3$), 1.02 (3H, s, 19-H$_3$), 3.33 (3H, s, –OCH$_3$), 3.58 (1H, m, 6-H), 4.55 (4H, m, –OCH$_2$O–, =CH$_2$).

3β-Methyl-5α-cholestan-6-one (38)——The olefin **36** (300 mg, 0.676 mmol) was hydrogenated, as described for **18**, to give 6β-methoxymethoxy-3β-methyl-5α-cholestane (300 mg). This in THF (5 ml) was treated with conc. HCl (0.2 ml) at 50 °C for 5 h. Work-up (ether) gave a crude product, which was oxidized with Jones reagent to give the 3β-methyl steroid **38** (260 mg, 98%), mp 102—104 °C (MeOH). ^{1}H-NMR δ: 0.65 (3H, s, 18-H$_3$), 0.68 (3H, s, 19-H$_3$), 0.85 (6H, d, J=6 Hz, 26-H$_3$, 27-H$_3$). *Anal.* Calcd for $C_{28}H_{48}O$: C, 83.93; H, 12.07. Found: C, 83.87; H, 12.01.

3α- and 3β-Acetoxymethyl-5α-cholestan-6-one (42 and 41)——The olefin **36** (1.0 g, 2.25 mmol) in THF (10 ml) was treated with 1 M BH_3–THF complex solution (6 ml) at room temperature for 1.5 h. Water was carefully added to decompose the excess reagent. Then, 2 M NaOH (3 ml) and 30% H_2O_2 (3 ml) were added. Stirring was continued at room temperature for 1 h. Work-up (ether) followed by acetylation with acetic anhydride (4 ml) and pyridine (5 ml) at room temperature for 18 h gave two separable products. Work-up (EtOAc) and chromatography on silica gel (50 g) with benzene–EtOAc (100 : 1) gave the less polar product **40** (570 mg, 50%) and the more polar product **39** (310 mg, 27%).

The less polar acetate **40** (570 mg) in THF (10 ml) was treated with 6 M HCl (2 ml) at room temperature for 15 h and then treated with Jones reagent in acetone (10 ml). Work-up (ether) and chromatography on silica gel (30 g) with benzene–EtOAc (100 : 1) gave the 3α-compound **42**, mp 68—72 °C (MeOH–ether). ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.74 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 2.02 (3H, s, acetyl), 4.04 (2H, d, J=8 Hz, –C$\underline{H}_2$–OAc). *Anal.* Calcd for $C_{30}H_{50}O_3$: C, 78.55; H, 10.99. Found: C, 78.47; H, 10.92.

The more polar acetate **39** (310 mg) was similarly converted into the 6-oxo compound **41** (210 mg, 71%), amorphous solid. ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.70 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 2.02 (3H, s, acetyl), 3.90 (2H, d, J=5 Hz, –C$\underline{H}_2$–OAc).

6β-Methoxymethoxy-5α-cholest-2-ene (43)——5α-Cholest-2-en-6-one (**17**) (17 g, 44.3 mmol) in THF (300 ml) was treated with lithium aluminum hydride (2.0 g, 52.6 mmol) at room temperature for 1 h. Water was carefully added to decompose the excess hydride. Filtration and removal of the solvent gave a crude product (17 g). This crude product was dissolved in dioxane (260 mg) and diethylcyclohexylamine (25 ml). Chloromethyl methyl ether (10 ml) was added to the solution. The mixture was stirred at 50 °C for 3 h. Work-up (ether) and chromatography on silica gel (100 g) with benzene gave the product **43** (15.2 g, 80%), mp 75—76 °C (MeOH). ^{1}H-NMR δ: 0.68 (3H, s, 18-H_3), 0.88 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.92 (3H, s, 19-H_3), 3.37 (3H, s, –OCH_3), 3.66 (1H, m, $W_{1/2}$=8 Hz, 6α-H), 4.63 (2H, dd, J=10, 7 Hz, –OCH_2O–), 5.52 (2H, m, 2-H, 3-H). *Anal.* Calcd for $C_{29}H_{50}O_2$: C, 80.87; H, 11.70. Found: C, 80.94; H, 11.66.

6β-Methoxymethoxy-5α-cholestan-2β-ol (44)——The 2-ene **43** (8.8 g, 20.5 mmol) in glyme–H_2O (15 : 1, 160 ml) was treated with *N*-bromosuccinimide (5.0 g, 24.5 mmol) at room temperature for 1 h. Work-up (ether) gave a crude product, which in THF (150 ml) was treated with lithium aluminum hydride (1.5 g, 39.5 mmol) under reflux for 2 h. Work-up (ether) and chromatography on silica gel (50 g) with benzene–EtOAc (50 : 1) gave the 2β-ol **44** (5.5 g, 60%), mp 140—141 °C (MeOH). ^{1}H-NMR δ: 0.69 (3H, s, 18-H_3), 0.88 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.91 (3H, s, 19-H_3), 3.37 (3H, s, –OCH_3), 3.65 (1H, m, $W_{1/2}$=8 Hz, 6-H), 4.15 (1H, m, $W_{1/2}$=8 Hz, 2α-H), 4.62 (1H, dd, J=10, 7 Hz, –OCH_2O–). *Anal.* Calcd for $C_{29}H_{52}O_3$: C, 77.62; H, 11.68. Found: C, 77.85; H, 11.50.

2β-Acetoxy-5α-cholestan-6-one (46)——The 2β-ol **44** (3.14 g, 7.0 mmol) in pyridine (7 ml) was treated with acetic anhydride (5 ml) at room temperature overnight. Work-up (EtOAc) gave a crude product (3.3 g). This in THF (60 ml) was treated with 6 M HCl (6 ml) at 50 °C for 3 h. Work-up (ether) gave a crude product, which was dissolved in CH_2Cl_2 (100 ml). Then, sodium acetate (800 mg) and pyridinium chlorochromate (2.4 g, 11.2 mmol) were added to the solution. The reaction mixture was stirred at room temperature for 30 min, and ether (500 ml) was added. Filtration through a column of Florisil (20 g), elution with ether, and removal of the solvent gave a crude product (2.8 g). Chromatography on silica gel (40 g) with benzene–EtOAc (100 : 1) gave the 2β-acetoxy-6-ketone **46** (2.4 g, 77%), mp 154—155 °C (MeOH). ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.84 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.88 (3H, s, 19-H_3), 2.00 (3H, s, acetyl), 5.05 (1H, m, $W_{1/2}$=9 Hz, 2α-H). *Anal.* Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.58; H, 10.79.

2β-Hydroxy-5α-cholestan-6-one (47) and 2β-Hydroxy-5β-cholestan-6-one (48)——The acetate **46** (4.6 g, 10.3 mmol) in THF–MeOH (1 : 1, 60 ml) was treated with 5% KOH/MeOH (10 ml) under reflux for 1 h. Work-up (ether) and chromatography on silica gel (150 g) with benzene–EtOAc (25 : 1) gave the less polar 5α-steroid **47** (780 mg, 19%), mp 196—197 °C (MeOH). ^{1}H-NMR δ: 0.68 (3H, s, 18-H_3), 0.86 (6H, d, J=6.5 Hz, 26-H_3, 27-H_3), 1.00 (3H, s, 19-H_3), 0.90 (3H, d, J=6 Hz, 21-H_3), 4.16 (1H, m, $W_{1/2}$=9 Hz, 2α-H). *Anal.* Calcd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.64; H, 11.55.

Further elution with the same solvent gave the more polar 5β-steroid **48** (2.86 g, 69%), amorphous solid. ^{1}H-NMR δ: 0.66 (3H, s, 18-H_3), 0.86 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.91 (3H, d, J=6 Hz, 21-H_3), 0.92 (3H, s, 19-H_3), 3.76 (1H, m, $W_{1/2}$=24 Hz, 2α-H). *Anal.* Calcd for $V_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.61; H, 11.57.

2β-Trifluoroacetoxy-5α-cholestan-6-one (49)——The 2β-ol **47** (94 mg, 0.234 mmol) was converted, as described for **15**, into the trifluoroacetate **49** (105 mg, 80%), mp 176—177 °C (acetone). ^{1}H-NMR δ: 0.64 (3H, s, 18-H_3), 0.88 (3H, s, 19-H_3), 5.30 (1H, m, $W_{1/2}$=8 Hz, 2α-H). *Anal.* Calcd for $C_{29}H_{45}F_3O_3$: C, 69.85; H, 9.10. Found: C, 70.02; H, 9.14.

2β-*p*-Toluenesulfonyloxy-5α-cholestan-6-one (50)——The 2β-ol **47** (100 mg, 0.249 mmol) was converted, as described for **16**, into the tosylate **50** (115 mg, 83%), mp 153—155 °C (MeOH–ether). ^{1}H-NMR δ: 0.62 (3H, s, 18-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.98 (3H, s, 19-H_3), 2.40 (3H, s, tosyl), 5.43 (1H, m, $W_{1/2}$=8 Hz, 2α-H), 7.30 (2H, d, J=8 Hz, tosyl), 7.72 (2H, d, J=8 Hz, tosyl). *Anal.* Calcd for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41. Found: C, 73.28; H, 9.56.

6β-Methoxymethoxy-5α-cholestan-2-one (51)——The 2β-ol **44** (3.0 g, 6.72 mmol) in acetone (50 ml) was treated with 1 eq of Jones reagent at room temperature for 10 min. Work-up (ether) gave the 2-oxo steroid **51** (3.0 g), mp 89—90 °C (MeOH). IR ν_{max} cm^{-1}: 1710. ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.84 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.89 (3H, s, 19-H_3), 3.29 (3H, s, –OCH_3), 3.70 (1H, m, $W_{1/2}$=8 Hz, 6-H), 4.55 (2H, dd, J=10, 7 Hz, –OCH_2O–). *Anal.* Calcd for $C_{29}H_{50}O_3$: C, 77.97; H, 11.28. Found: C, 78.15; H, 11.06.

2α-Acetoxy-6β-methoxymethoxy-5α-cholestane (52)——A solution of the 2-oxo steroid **51** (2.76 g, 6.18 mmol) in THF (80 ml) was added to a solution of liquid ammonia (160 ml) and ethanol (10 ml) at −78 °C under an argon atmosphere. Then, small pieces of lithium (2.0 g) were added portionwise. The mixture was stirred at −78 °C for

30 min. Then, dry ammonium chloride (50 g) was added portionwise to the reaction mixture at −78 °C. Work-up (ether) gave a crude product, which in pyridine (20 ml) was treated with acetic anhydride (10 ml) at room temperature overnight. Work-up (EtOAc) and chromatography on silica gel (60 g) with benzene gave the 2α-acetate **52** (2.62 g, 91%), mp 79—80 °C (MeOH). ^{1}H-NMR δ: 0.69 (3H, s, 18-H_3), 0.86 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 1.02 (3H, s, 19-H_3), 1.99 (3H, s, acetyl), 3.30 (3H, s, –OCH_3), 3.60 (1H, m, $W_{1/2}$=7 Hz, 6α-H), 4.50 (2H, dd, J=10, 7 Hz, –OCH_2O–), 4.85 (1H, m, $W_{1/2}$=24 Hz, 2β-H). *Anal.* Calcd for $C_{31}H_{54}O_4$: C, 75.87; H, 11.09. Found: C, 75.32; H, 11.03.

2α-Acetoxy-5α-cholestan-6-one (53)——The methoxymethoxy ether **52** (2.4 g, 4.92 mmol) was deprotected and oxidized, as described for **42**, to give the 6-oxo steroid **53** (2.08 g, 95%), mp 154—156 °C (MeOH). ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.79 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 2.01 (3H, s, acetyl), 4.91 (1H, m, $W_{1/2}$=24 Hz, 2β-H). *Anal.* Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.47; H, 10.84.

2α-Hydroxy-5α-cholestan-6-one (54)——The acetate **53** (790 mg, 1.78 mmol) in THF–MeOH (2:1, 30 ml) was treated with 5% KOH/MeOH (4 ml) at room temperature for 1 h. Work-up (ether) gave the 2α-ol **54** (715 mg), mp 162—164 °C (MeOH). ^{1}H-NMR δ: 0.66 (3H, s, 18-H_3), 0.74 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 3.72 (1H, m, 2-H). *Anal.* Calcd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.77; H, 11.36.

2α-Trifluoroacetoxy-5α-cholestan-6-one (55)——The 2α-ol **53** (145 mg, 0.361 mmol) was converted, as described for **15**, into the trifluoroacetate **55** (178 mg, 98%), mp 136—137.5 °C (MeOH). ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.80 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 5.05 (1H, m, 2-H). *Anal.* Calcd for $C_{29}H_{45}F_3O_3$: C, 69.85; H, 9.10. Found: C, 69.94; H, 9.08.

2α-*p*-Toluenesulfonyloxy-5α-cholestan-6-one (56)——The 2α-ol **54** (145 mg, 0.361 mmol) was converted, as described for **16**, into the tosylate **56** (180 mg, 93%), mp 178—180 °C (MeOH). ^{1}H-NMR δ: 0.63 (3H, s, 18-H_3), 0.69 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 2.45 (3H, s, tosyl), 4.60 (1H, m, 2-H), 7.32 (2H, d, J=8 Hz, tosyl), 7.78 (2H, d, J=8 Hz, tosyl). *Anal.* Calcd for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41. Found: C, 73.29; H, 9.43.

1α-Methoxymethoxy-5α-cholestan-6β-ol (59)——The allylic alcohol **57**[6] (2.63 g, 5.92 mmol) in EtOAc (100 ml) was hydrogenated with 5% Pd–C (50 mg) at room temperature under a hydrogen atmosphere overnight. Filtration and removal of the solvent gave the saturated compound **58** (2.63 g), oil. ^{1}H-NMR δ: 0.69 (3H, s, 18-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.94 (3H, s, 19-H_3), 2.03 (3H, s, acetyl), 3.65 (1H, m, $W_{1/2}$=6 Hz, 1β-H), 5.08 (1H, m, $W_{1/2}$=8 Hz, 6α-H). This product was dissolved in dioxane (20 ml) and diethylcyclohexylamine (10 ml). Then, chloromethyl methyl ether (4 ml) was added to the solution. The mixture was stirred at 50 °C for 3 h. Work-up (EtOAc) gave a crude product, which in dioxane (20 ml) was treated with 5% KOH/MeOH (10 ml) under reflux overnight. Work-up (ether) and chromatography on silica gel (50 g) with benzene–EtOAc (100:1) gave the 6β-ol **59** (2.12 g, 80%), oil. ^{1}H-NMR δ: 0.68 (3H, s, 18-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 0.97 (3H, s, 19-H_3), 3.39 (3H, s, –OCH_3), 3.83 (1H, m, $W_{1/2}$=8 Hz, 1β-H), 4.50 (2H, dd, J=10, 7 Hz, –OCH_2O–).

1α-Hydroxy-5α-cholestan-6-one (60)——The 6β-ol **59** (2.1 g, 4.69 mmol) in acetone (50 ml) was treated with Jones reagent (1 eq) at room temperature for 10 min. Work-up (ether) gave a crude product, which in THF (30 ml) was treated with 6 M HCl (6 ml) at room temperature overnight. Work-up (ether) and chromatography on silica gel (50 g) with benzene–EtOAc (50:1) gave the 1α-ol **60** (1.8 g, 95%), mp 186—187 °C (acetone). IR ν_{max} cm^{-1}: 1713. ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.73 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 3.76 (1H, m, $W_{1/2}$=8 Hz, 1β-H). *Anal.* Calcd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.61; H, 11.31.

1α-Acetoxy-5α-cholestan-6-one (61)——The 1α-ol **60** (184 mg, 0.458 mmol) was acetylated with pyridine (2 ml) and acetic anhydride (1 ml) at room temperature overnight. Work-up (EtOAc) and chromatography gave the 1α-acetate **61** (172 mg, 85%), mp 105—106 °C (MeOH). ^{1}H-NMR δ: 0.65 (3H, s, 18-H_3), 0.80 (3H, s, 19-H_3), 0.86 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 2.08 (3H, s, acetyl), 4.85 (1H, m, $W_{1/2}$=6 Hz, 1β-H). *Anal.* Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.28; H, 10.70.

1α-Trifluoroacetoxy-5α-cholestan-6-one (62)——The 1α-ol **60** (184 mg, 0.458 mmol) was converted, as described for **15**, into the trifluoroacetate **62** (240 mg, 98%), mp 107—108 °C (MeOH). ^{1}H-NMR δ: 0.64 (3H, s, 18-H_3), 0.82 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 5.05 (1H, m, $W_{1/2}$=6 Hz, 1β-H). *Anal.* Calcd for $C_{29}H_{45}F_3O_3$: C, 69.85; H, 9.10. Found: C, 70.15; H, 8.94.

1α-*p*-Toluenesulfonyloxy-5α-cholestan-6-one (63)——The 1α-ol **60** (180 mg, 0.448 mmol) was converted, as described for **16**, into the tosylate **63** (236 mg, 95%), mp 139—141 °C (MeOH). ^{1}H-NMR δ: 0.62 (3H, s, 18-H_3), 0.75 (3H, s, 19-H_3), 0.85 (6H, d, J=6 Hz, 26-H_3, 27-H_3), 2.42 (3H, s, tosyl), 4.78 (1H, m, $W_{1/2}$=6 Hz, 1β-H), 7.35 (2H, d, J=8 Hz, tosyl), 7.80 (2H, d, J=8 Hz, tosyl). *Anal.* Calcd for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41. Found: C, 73.09; H, 9.37.

References

1) *a*) R. C. Cookson, R. P. Gandhi, and R. M. Southam, *J. Chem. Soc. C*, **1968**, 2494; *b*) M. S. Ahmad, G. Moinuddin, and I. A. Khan, *J. Org. Chem.*, **43**, 163 (1978).

2) *a*) M. Ishiguro, S. Takatsuto, M. Morisaki, and N. Ikekawa, *J. Chem. Soc., Chem. Commun.*, **1980**, 962; *b*) S. Takatsuto, N. Yazawa, M. Ishiguro, M. Morisaki, and N. Ikekawa, *J. Chem. Soc., Perkin Trans. 1*, **1984**, 139; The high regio-selectivity was also pointed out by other groups; *c*) M. J. Thompson, N. B. Mandava, J. L. Flippen-Anderson, J. F. Worley, S. R. Dutky, W. E. Robbins, and W. R. Lusby, *J. Org. Chem.*, **44**, 5002 (1979);

d) S. Fung and J. B. Siddall, *J. Am. Chem. Soc.*, **102**, 6580 (1980).
3) S. Takatsuto and N. Ikekawa, *Tetrahedron Lett.*, **24**, 917 (1983).
4) M. Morisaki, A. Saika, K. Bannai, M. Sawamura, J. Rubio-Lightbourn, and N. Ikekawa, *Chem. Pharm. Bull.*, **23**, 3272 (1975).
5) D. N. Jones, R. Grayshan, A. Hinchcliffe, and D. E. Kime, *J. Chem. Soc. C*, **1969**, 1208.
6) M. Ishiguro, A. Kajikawa, T. Haruyama, Y. Ogura, M. Okubayashi, M. Morisaki, and N. Ikekawa, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 2295.