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A-Substituted 5β-Steroids. III. Synthesis of 2-Oxo-5β-steroids and Their Derivatives

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The synthesis of 2-oxo-5β-steroids (5β-cholestan-2-one and methyl 2-oxocholanate) and their derivatives have been described. Both oxo-steroids were prepared from 2β-acetoxy-3-oxo-5β-steroids according to the following synthetic pathways: (a) condensation with ethylmercaptan to diethylmercaptol, desulfurization, hydrolysis and oxidation, (b) condensation with ethylmercaptan to diethylmercaptol, hydrolysis to hydroxy-ethylmercaptol, desulfurization and oxidation, and (c) isomerisation to 3α-acetoxy-2-oxo derivative and deacetylation with zinc powder to 2-oxo derivative. In these pathways, it was found that method (b) gave the best yield. On the other hand, desulfurization of the hydroxy-mercaptols with one-half the weight of Raney nickel used for that of method (b) gave 2β-hydroxy-3β-ethylthio derivatives as intermediates. Reductive cleavage of these hydroxy-ethylthio derivatives with Raney nickel produced 2β-hydroxy-5β-steroids in good yields. In the halogenation of these 2-oxo derivatives, the products were 1β-halo-2-oxo-5β-sterodis, not 1α- or 3-halo isomers.

Although most 5α-steroids which possess subtituents on each position in ring A have been thoroughly investigated,[1] only very little information is found in literature concerning the synthesis of 1- and 2-substituted 5β-steroids.[2] On the synthesis of 2-substituted 5β-steroid, Tomoeda and Koga[3] recently repoted that 2α-hydroxy-5β-chloestane was obtained from 4β,5β-epoxycholestan-3-one through

1) L. F. Fieser and M. Fieser, "Steroids," Reinhold Pub. Inc., New York (1959), p. 169; C. Djerassi, "Steroids Reactions," Holden-Day, Inc., San Francisco (1963), pp. 181, 537.

2) Y. Satoh, T. Takahashi, T. Aoki and A. Hagitani, This Bulletin, **42**, 1465 (1969).

3) M. Tomoeda and T. Koga, *Tetrahedron Lett.*, **1965**, 3231.

the epoxy ring opening, condensation with ethanedithiol to an ethylene thioketal, desulfurization, and hydrogenation.

During the course of our studies of A-substituted 5β-steroids, we have found that the substitution reaction of 4β-bromo-3-oxo-5β-steroids (1) with potassium acetate and acetic acid is accompanied with a new rearrangement of a substituent from C_4 to C_2 resulting in the 2β-acetoxy-3-oxo derivative (2) in good yield.[4] In our previous communication, we also reported that the bromination of 2-oxo-5β-steroids affords the 1β-bromo-2-oxo-5β-steroids.[5] In the present paper, we wish to describe in full the details for the synthesis of 1-haloketones from 2β-acetoxy-3-oxo-5β-steroids (2).

Condensation with ethyl mercaptan to diethylmercaptols (3) of the acetoxyketones (2) and hydrogenation of the mercaptols with Raney nickel (W-2) gave acetoxy compounds corresponding in spectroscopic properties to 2β-acetoxy-5β-steroids (4).

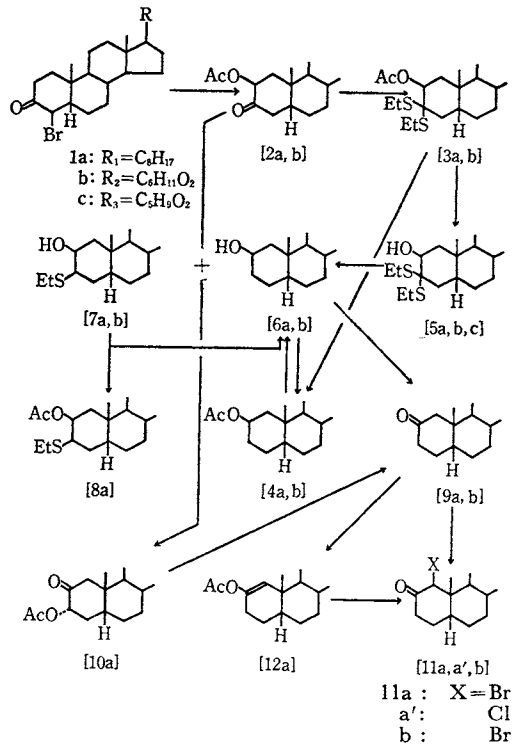
In the desulfurization method, considerable amounts of saturated 5β-steroids were formed, and so we attempted another route for the deketonisation; that is, the derivatives (3) were converted to 2β-hydroxy-3-oxo diethylmercaptols (5) by alkaline hydrolysis. In the case of (3b), however, the carbomethoxy group in the side chain was hydrolyzed to carboxylic acid (5c) and then the acid was converted to its methyl ester (5b) with diazomethane. By desulfurization of these 2β-hydroxy-3-oxo-5β-steroid diethylmercaptols with Raney nickel according to the same method for (3), 2β-hydroxy-5β-steroids were formed in good yield. The configuration of these products has been determined by IR spectra and the patterns of NMR spectra. The total yields of 2β-hydroxy-5β-steroids from the 2β-acetoxy-3-oxo-5β-steroids were 80 and 44% (cholestane and 3-bile acid series, respectively).

Acetylation of the 2β-hydroxy-5β-steroids with acetic anhydride and pyridine produced 2β-acetoxy derivatives (4), identical with the specimens described above. In the NMR spectra of 2β-hydroxy- and 2β-acetoxy-5β-cholestanes, it was found that the signals due to C_2-αH were shifted more to the the upper field than those of 2α-isomers.[3] This agreed with the relation of the chemical shifts between *a*- and *e*-H due to the anisotropy of C–C linkage in cyclohexane ring.[6]

When the desulfurization of the hydroxy diethylmercaptols (5) was carried out with one-half the weight of Raney nickel used for that of (3), 2-hydroxy-3-ethylthio derivatives (7) were obtained as intermediates. Small amounts of 2-oxo- and 2β-hydroxy-5β-steroids were also formed. One of the products (7b) could be isolated as needles, but it was so difficult to crystallize the other product (7a) that it was converted to its acetate (8) by treatment with acetic anhydride and pyridine. In the NMR spectra of both crystalline products, (8) has a multiplet at τ 6.60 (Hw=8 Hz, 1H) and a sextet at τ 4.97 (J=4.5, and 10.5 Hz, 1H) and (7b) has multiplets at τ 6.88 (Hw=8 Hz, 1H) and near τ 4.2.*1 From these data, it was found that the intermediates obtained from the desulfurization were 2β-hydroxy-3β-ethylthio-5β-steroids. The reductive cleavages of these hydroxy-ethylthio derivatives with Raney nickel produced 2β-hydroxy-5β-steroids in good yields.

Oxidation of the 2β-hydroxy-5β-steroids with chromic acid and acetic acid gave 2-oxo-5β-steroids (9) showing a double Cotton curve near 310 mμ. One of the products was identical with 5β-cholestan-2-one prepared by Tomoeda and Koga.[3]

In a previous paper, it was reported that the isomerisation of 2β-acetoxy-5β-cholestan-3-one with hydrogen bromide and acetic acid gave 3α-acetoxy-5β-cholestan-2-one (10).[7] In general, α-ketols and their acetates are reduced to the ketone with zinc



*1 This signal owing to C_2-αH could not be clarified, because it was overlapped by the CH_3-signal of the C_{24}-carbomethoxy group.

4) T. Takahashi, Y. Satoh and A. Hagitani, *Nippon Kagaku Zasshi*, **89**, 974 (1968).

5) Y. Satoh, A. Horiuchi, T. Matsukura and A. Hagitani, This Bulletin, **41**, 3032 (1968).

6) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein and W. G. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958); N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco (1964), p. 49.

7) Y. Satoh, T. Kimura, Y. Tajima, T. Takahashi and A. Hagitani, *Nippon Kagaku Zasshi*, **90**, 500 (1969).

and acetic acid.[8] Therefore, the synthesis of 5β-cholestan-2-one from the 3α-acetoxy-2-oxo derivative (10) has been studied according to this method. In a small scale experiment, satisfactory result was obtained, but in a large scale experiment, zinc in great bulk prevented stirring, so that this method was not practical for the synthesis of 5β-cholestan-2-one.

In the bromination of the 2-oxo derivatives, the products were 1β-bromo-2-oxo-5β-steroids, not 1α- or 3-bromo isomers. This was determined by signs of the Cotton effect, Δ[A] (+233 for 5β-cholestan-2-one and +164 for methyl 2-oxocholanate) and $\Delta\lambda_1$-values (+20 and +18 mμ, respectively) in ORD, the shifts of C=O stretching bands (+4 and +2 cm^{-1}, respectively) in IR spectra and the patterns of the NMR spectra.

In connection with the above investigation, we carried out the enol acetylation of 5β-cholestan-2-one according to the directions of Djerassi *et al.* described for the 5α-series.[9] On chromatographical separation of the reaction product, 5β-cholest-1-en-2-ol acetate was obtained. It was found, moreover, that bromination of this enol acetate with bromine in acetic acid gave the same product as described above for that of 5β-cholestan-2-one. From these results, we may conclude that the enolization of the 2-oxo-5β-steroids occurs in the direction of C_1, not C_3, and that the bromination of these ketones forms the 1β-bromo-2-oxo derivatives. The configuration of these bromoketones is consistent with Corey's prediction for the 2-oxo-5β-steroid.[10]

Chlorination of 5β-cholestan-2-one also produced 1β-substituted derivative as in the case of bromination. In the NMR spectra of both 1β-haloketones, it was found that the signal due to C_1-αH in the chloroketone was shifted more to the upper field than that of the bromoketone.

Experimental

Instrumentation. IR and ORD spectra were measured on a Shimadzu model IR-27B infrared spectrometer and a JASCO model ORD/UV-5 spectrometer, respectively. NMR spectra were recorded in deuterochloroform, with TMS as the internal standard with a JEOL model JNM-4H-100 high resolution nuclear spectrometer.

2β-Acetoxy-5β-cholestan-3-one Diethylmercaptol (3a). A current of dry hydrogen chloride was passed into a mixture of (2a) (19.0 g) and ethyl mercaptan (24 m*l*) under cooling with an ice-bath for 10 min. After the reaction mixture had stood for 15.5 hr in a refrigerator, the excess of ethyl mercaptan was removed in a vacuum desiccator on sodium hydroxide. The resulting oil was then extracted with ether. The ether extracts were washed with sodium hydrogencarbonate solution and water, dried, and evaporated under reduced pressure. A slightly brownish oil (21.7 g) was obtained. Attempts to crystallize the diethylmercaptol were unsuccessful, and so it was used in the next step without purification. ν_{max}^{Film} cm^{-1}: 1745 (C=O), 1234 (C-O), 770 (C-S).

Methyl 2β-Acetoxy-3-oxocholanate Diethylmercaptol (3b). The method used here was identical with that described for (3a). No crystalline diethylmercaptol (22.0 g) was obtained from methyl 2β-acetoxy-3-oxocholanate (16.5 g). ν_{max}^{Film} cm^{-1}: 1733 (C=O), 1230, 1165 (C-O), 771 (C-S).

2β-Acetoxy-5β-cholestane (4a). A solution of diethylmercaptol (3a) (9 g) in methanol-acetone (1 : 1, 400 m*l*) was refluxed with Raney nickel (W-2, 90 g) under effecient stirring for 2.5 hr. The hot reaction mixture was filtered and the clear filtrate was evaporated under reduced pressure. The resulting oil (7 g) was chromatographed on silica gel; 5β-cholestane was first eluted by petroleum ether, and the next fraction eluted with benzene - petroleum ether (2 : 1), on crystallization from ethanol gave plates of 2β-acetoxy-5β-cholestane (1.7 g), mp 59—61.5°C, $[\alpha]_D^{24}$ +19.7°C (*c* 1.26, $CHCl_3$), NMR ($CDCl_3$) τ: 5.23 (septet, *J*=5.5 and 11 Hz, 1H), ν_{max}^{KBr} cm^{-1}: 1732 (C=O), 1240 (C-O).

Found: C, 80.55; H, 11.62%. Calcd for $C_{29}H_{50}O_2$: C, 80.87; H, 11.71%.

Methyl 2β-Acetoxycholanate (4b). The desulfurization of the diethylmercaptol (3b) (7.1 g) was carried out using the technique described for the synthesis of (4a). The resulting oil (5.4 g) from the reaction mixture was chromatographed on silica gel; benzene eluted a yellow oil which on crystallization from methanol gave needles of methyl cholanate (3.6 g), mp 85—87°C. The next fraction, eluted by the same solvent, on crystallization from methanol gave plates of methyl 2β-acetoxycholanate (0.3 g), mp 75.5—77°C, $[\alpha]_D^{24}$ +17.9° (*c* 1.12, $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 1739, 1725 (C=O), 1255, 1173 (C-O), NMR ($CDCl_3$) τ: 5.21 (septet, *J*=6.5 and 13 Hz, 1H), 6.36 (s., 3H), 8.01 (s., 3H).

Found: C, 75.33; H, 10.39%. Calcd for $C_{27}H_{44}O_4$; C, 74.96; H, 10.25%.

2β-Hydroxy-5β-cholestan-3-one Diethylmercaptol (5a). A mixture consisting of (4a) (21.7 g), sodium hydroxide (2.4 g), water (2 m*l*), and methanol (800 m*l*) was refluxed for 4.5 hr. After evaporation of the reaction mixture, the residue was dissolved in ether. The ethereal solution was washed with water, dried, and evaporated. Crystallization of the resulting oil from ethanol gave 2β-hydroxy-5β-cholestan-3-one diethylmercaptol as needles (16 g), mp 79—80.5°C, $[\alpha]_D^{24}$ +15.0° (*c* 1.00, $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 3420 (O-H), 770 (C-S), NMR ($CDCl_3$) τ: 6.44 (t., *J*=5 and 10 Hz, 1H), 7.28 (m., 4H).

Found: C, 73.47; H, 11.06; S, 12.49%. Calcd for $C_{31}H_{56}OS_2$: C, 73,16; H, 11.09; S, 12.60%.

Methyl 2β-Hydroxy-3-oxocholanate Diethylmercaptol (5b). A solution of (3b) (6.09 g) in methanol (200 m*l*) was refluxed with potassium hydroxide (2 g) in water (15 m*l*) for 6 hr. After cooling, the reaction mixture was poured into ice-water and acidified with dilute hydrochloric acid. The resulting precipitate

8) R. S. Rosenfeld, *J. Amer. Chem. Soc.*, **79**, 5540 (1957); R. L. Augustine, "Reduction," Marceldekker, Inc., New York (1968), p. 140.

9) C. Djerassi and T. Nakano, *Chem. Ind.*, **1960**, 1385; T. Nakano, M. Hasegawa and C. Djerassi, *Chem. Pharm. Bull.* (Tokyo), **11**, 465 (1962).

10) E. J. Corey, *J. Amer. Chem. Soc.*, **75**, 2301 (1953); **76**, 175 (1954).

was taken up in ether and the ether extracts were washed with water, dilute sodium hydrogencarbonate solution, then water, dried, and concentrated. Crystallization of the residue from methanol gave needles of 2β-hydroxy-3-oxocholanic acid diethylmercaptol (5c) (4.77 g), mp 152—154°C, $[\alpha]_D^{26}$ +12.4° (*c* 0.97, $CHCl_3$).

The acid (5c) (4 g) was converted to its methyl ester with diazomethane. After evaporation of the solvent, crystallization of the residue from methanol gave methyl ester (5b) (2.98 g), mp 89—90.5°C, $[\alpha]_D^{24}$ +13.5° (*c* 1.13, $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 3450 (O–H), 1735 (C=O), 1166 (C–O), 765 (C–S).

Found: C, 68.32; H, 9.70; S, 12.51%. Calcd for $C_{29}H_{50}O_3S_2$: C, 68.19; H, 9.87; S, 12.55%.

From the mother liquor, a second crop (0.79 g), mp 81.5—85°C, was also obtained.

2β-Hydroxy-5β-cholestane (6a). (i) A solution of 2β-acetoxy-5β-cholestane (4a) (1.4 g) in methanol (5.6 m*l*) and ether (10 m*l*) was refluxed with sodium hydroxide (0.36 g) in water (1.4 m*l*) for 3 hr. After evaporation of the reaction mixture, the residue was dissolved in ether. The ethereal solution was washed with water, dried, and evaporated. Crystallization of the residue from ethanol gave needles of (6a) (0.91 g), mp 100—104°C, $[\alpha]_D^{24.5}$ +14.9° (*c* 0.93, $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 3300 (O–H), NMR ($CDCl_3$) τ: 6.28 (septet, *J*=5 and 10 Hz, 1H).

Found: C, 83.10; H, 12.41%. Calcd for $C_{27}H_{48}O$: C, 83.43; H, 12.45%.

(ii) 2β-Hydroxy-5β-cholestan-3-one diethylmercaptol (5a) (12.2 g) was treated with Raney nickel according to the method for the synthesis of (4a) from (3a). Attempts to crystallize the residue were unsuccessful, but this product was identical with 2β-hydroxy-5β-cholestane prepared by the method (i) in t.l.c., g.l.c., and IR spectrum. Acetylation of a part of the product gave 2β-acetoxy-5β-cholestane as plates, which was identical with the specimen prepared from 2β-acetoxy-5β-cholestan-3-one diethylmercaptol with Raney nickel. Thus the oily product was used for the synthesis of 5β-cholestan-2-one (9a) without further purification.

Methyl 2β-Hydroxycholanate (6b). A mixture of (5b) (6.15 g), methanol-acetone, and Raney nickel was treated by the same method as for (6a) (method ii). The resulting oil (4.75 g) was chromatographed on silica gel. A small amount of methyl 2-oxocholanate was first eluted with benzene-ether (20 : 1), and a second fraction, eluted with the same solvent, on crystallization from methanol gave plates of methyl 2β-hydroxycholanate (2.5 g), mp 80—81°C, $[\alpha]_D^{24}$ +10.5° (*c* 0.96, $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 3420 (O–H), 1737 (C=O), 1166 (C–O).

Found: C, 76.84; H, 10.76%. Calcd for $C_{25}H_{42}O_3$: C, 76.87; H, 10.84%.

Acetylation of the product (6b) in the usual method produced methyl 2β-acetoxycholanate, which was identical with the product prepared from the mercaptol (3b) by desulfurization.

2β-Acetoxy-3β-ethylthio-5β-cholestane (8a). A solution of (5a) (19.5 g) in methanol-acetone (1 : 1, 300 m*l*) was refluxed with one-half the weight of Raney nickel used for the synthesis of 2β-hydroxy-5β-steroid from diethylmercaptol (5). After 30 min, the reaction mixture was filtered and evaporated. On chromatography of the residue with silica gel, benzene - petroleum ether eluted an oil (5.38 g), which consisted of 2β-hydroxy-3β-ethylthio-5β-cholestane (7a) and 5β-cholestan-2-one (9a). Isolation of (7a) from the mixture was so difficult that the compound was converted to its acetate with acetic anhydride and pyridine. Recrystallization of the acetylation product from ethanol gave needles of 2β-acetoxy-3β-ethylthio-5β-cholestane (8a) (3.6 g), mp 66—68.5C°, $[\alpha]_D^{24}$ +2.5°C (*c* 1.22, $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 1744 (C=O), 1238 (C–O), 731 (C–S), NMR ($CDCl_3$) τ: 4.97 (sextet, *J*=4.5 and 10.5 Hz, 1H), 6.60 (m., Hw=8 Hz, 1H), 7.23—7.67 (q., –S– CH_2–), 7.93 (s., 3H).

Found: C, 76.23; H, 11.20; S, 6.45%. Calcd for $C_{31}H_{54}O_2S$: C, 75.86; H, 11.09; S, 6.53%.

Further desulfurization of the mixture consisting of (7a) and (9a) with Raney nickel produced needles of 2β-hydroxy-5β-cholestane.

Benzene eluted a yellow oil which on crystallization from ethanol gave 2α-hydroxy-5β-cholestane (3.7 g).

Methyl 2β-Hydroxy-3β-ethylthiochlolanate (7b). A solution of the diethylmercaptol (5b) (1g) in methanol-acetone (1 : 1, 30 m*l*) was treated with Raney nickel according to the procedure described for the synthesis of (7a) except that the reaction was carried out for 1 hr. On chromatography of the residue with silica gel, crystallization of benzene eluates gave needles of methyl 2β-hydroxy-3β-ethylthiocholanate (201 mg), mp 105.5—106.5°C, from methanol. $[\alpha]_D^{24}$ −27.3° (*c* 1.06, $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 3473 (O–H), 1746 (C=O), 1153 (C–O), 766 (C–S).

Found: C, 71.63; H, 10.32; S, 7.09%. Calcd for $C_{27}H_{46}O_3S$: C, 71.95; H, 10.29; S, 7.11%.

Desulfurization of the hydroxy-ethylthio derivative by the method used for (8a) gave methyl 2β-hydroxycholanate.

Further elution with benzene afforded a mixture consisting of a trace of methyl 2-oxo- (9b) and 2β-hydroxycholanate (6b).

5β-Cholestan-2-one (9a). (i) From 2β-Hydroxy-5β-cholestane (6a). A solution of (6a) (8.4 g) in acetic acid (160 m*l*) was treated with chromium trioxide (2.4 g) in 80% acetic acid (14 m*l*) at 10—15°C. After standing for 2 hr, a small amount of methanol was added to the reaction mixture. The solution was slightly warmed on a water bath, cooled, and poured into water, and the resulting precipitate was extracted with ether. The ether extracts were washed with sodium hydrogencarbonate solution and water, dried, and evaporated. Crystallization of the residue from ethanol gave plates of (9a) (5.9 g), mp 86—88°C, ν_{max}^{KBr} cm^{-1}: 1712 (C=O), ORD (*c* 0.49, Di) at 26°C: $[\alpha]_{589}$ +16.3°, $[\alpha]_{400}$ +24.5°, $[\alpha]_{370}$ 0°, $[\alpha]_{316}$ −321.5° (trough), $[\alpha]_{306}$ −244.9° (sh.), $[\alpha]_{302}$ 0°, $[\alpha]_{275}$ +263.3° (peak).

Found: C, 83.29; H, 11.81%. Calcd for $C_{27}H_{46}O$: C, 83.86; H, 11.99%.

(ii) From 3α-Acetoxy-5β-cholestan-2-one (10a). A mixture of (10a) (377 mg), zinc powder (37.7 g), and acetic acid (198 m*l*) was refluxed with stirring for 14 hr. After evaporation of the solvent, the residue was taken up into ether and the ether extracts were washed with sodium hydrogencarbonate solution and water, dried, and concentrated. Crystallization from ethanol gave plates of 5β-cholestan-2-one (50 mg), mp 85—87°C. This product was identical with a sample prepared by method (i) in IR and ORD spectra.

Methyl 2-Oxocholanate (9b). This substance was prepared according to method (i) described above for

the synthesis of (9a). The crystallization of the resulting oil from methanol gave needles of methyl 2-oxocholanate (819 mg), mp 88—89.5°C, from (6b) (1 g). ν_{max}^{KBr} cm^{-1}: 1733, 1708 (C=O), 1162 (C-O), ORD (*c* 0.59, Di) at 26°C: $[\alpha]_{589}$+20.3°, $[\alpha]_{400}$+31.6°, $[\alpha]_{357}$ 0°, $[\alpha]_{317}$ −273° (trough), $[\alpha]_{307}$ −166° (sh.), $[\alpha]_{302}$ 0°, $[\alpha]_{275}$ +509° (peak).

Found: C, 77.27; H, 10.38%. Calcd for $C_{25}H_{40}O_3$: C, 77.58; H, 10.49%.

1β-Bromo-5β-cholestan-2-one (11a). 5β-Cholestan-2-one (4.24 g) was dissolved in acetic acid (100 m*l*) and a few drops of 47% hydrogen bromide were added, followed by addition of bromine (1.75 g) in acetic acid (10 m*l*) with stirring for 25 min at 18°C. The reaction mixture was cooled, and the crystals formed were collected. The crystals were dissolved in ether and the ethereal solution was washed, dried, and evaporated. Crystallization of the residue from methanol-ether gave needles (3.82 g), mp 128—130°C, ν_{max}^{KBr} cm^{-1}: 1714 (C=O), 668 (C-Br), ORD (*c* 0.52, Di) at 26°C: $[\alpha]_{589}$ +9.6°, $[\alpha]_{400}$+421°, $[\alpha]_{336}$+2187° (peak), $[\alpha]_{314}$ 0°, $[\alpha]_{288}$ −2369° (trough), NMR ($CDCl_3$) τ: 5.68 (s., 1H).

Found: C, 69.78; H, 9.80%. Calcd for $C_{27}H_{45}OBr$: C, 69.65; H, 9.74%.

Methyl 1β-Bromo-2-oxocholanate (11b). Bromination of methyl 2-oxocholanate (834 mg) was carried out using the technique for the synthesis of (11a). The reaction mixture was taken up in ether and the ether extracts were washed, dried, and evaporated. On chromatography of the residue with silica gel, elution with benzene gave an oily product (650 mg). Crystallization of this product from methanol afforded needles (81 mg) of (11b), mp 138—140°C, ν_{max}^{KBr} cm^{-1}: 1735, 1710 (C=O), 1171 (C-O), 673 (C-Br), ORD (*c* 0.62, Di) at 25°C: $[\alpha]_{589}$+67.7°, $[\alpha]_{400}$+271°, $[\alpha]_{335}$+1394° (peak), $[\alpha]_{313}$ 0°, $[\alpha]_{289}$−1468° (trough), NMR ($CDCl_3$) τ: 5.66 (s., 1H), 6.35 (s., 3H).

Found: C, 63.33; H, 8.00%. Calcd for $C_{25}H_{39}O_3Br$: C, 64.24; H, 8.41%.

1β-Chloro-5β-cholestan-2-one (11a′). A solution of chlorine (79 mg) in chloroform (3 m*l*) was added to a mixture consisting of 5β-cholestan-2-one (9a) (386 mg), concd. hydrochloric acid (2 drops) and acetic acid (15 m*l*) with stirring at 20°C. After 15 min, the reaction mixture was poured into water, and the chloroform layer was washed, dried, and evaporated. Crystallization of the residue from methanol-acetone gave needles (247 mg), mp 116—118°C, ν_{max}^{KBr} cm^{-1}: 1721 (C=O), ORD (*c* 0.59, Di) at 25°C: $[\alpha]_{589}$+50.8°, $[\alpha]_{400}$+131.4°, $[\alpha]_{327}$+645.8° (peak), $[\alpha]_{321}$+557.6° (trough), $[\alpha]_{316}$+627.1° (peak), $[\alpha]_{298}$ 0°, $[\alpha]_{281}$−314.4° (trough), NMR ($CDCl_3$) τ: 5.83 (s., 1H).

Found: C, 76.49; H, 11.22%. Calcd for $C_{27}H_{45}OCl$: C, 77.01; H, 10.77%.

2-Acetoxy-5β-cholest-1-ene (12a). This substance was prepared according to the directions of Djerassi *et al.* described for 5α-isomer.[9] The reaction product was chromatographed in petroleum ether on silica gel. Elution with benzene gave needles of (12a) from ethanol, mp 103—105°C, $[\alpha]_D^{26}$+52.0°C (*c* 0.997, in $CHCl_3$), ν_{max}^{KBr} cm^{-1}: 1750 (C=O), 1687 (C=C), 1215 (C-O), NMR ($CDCl_3$) τ: 4.66 (s., 1H), 7.93 (s., 3H).

Found: C, 80.52; H, 11.01%. Calcd for $C_{29}H_{48}O_2$: C, 81.25; H, 11.29%.

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