A-Substituted 5β-Steroids. VIII. Synthesis and Bromination of 3-Alkyl-5β-cholestan-2-one

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3α-Alkyl-5β-cholestan-2-one (R=CH_3, C_2H_5, and $CH_3CH_2CH_2$) was prepared by the direct alkylation of 5β-cholestan-2-one with alkyl iodide and potassium *t*-butoxide in a reflux of *t*-butyl alcohol–benzene. The 3α-benzyl ketone was prepared from 5β-cholestan-2-one by aldol condensation with benzaldehyde in the presence of potassium hydroxide, followed by hydrogenation of the condensation product. The bromination of these 3α-alkyl ketones gave 3β-bromo-3α-alkyl-5β-cholestan-2-ones.

The alkylation of the steroids which have an oxo group in ring A has been investigated.[1–4] In addition, the preparation and use of hydroxymethylene derivatives of 5β-stigmast-22-en-3-one[5] and pregn-4-ene-3,20-dione[6] have been described.

Recently, as a part of our studies on the A-substituted 5β-steroids, we reported the halogenation[7] of 5β-cholestan-2-one and some reactions[7] of their halo ketones. In the present paper, the direct alkylation of 5β-cholestan-2-one with alkyl iodide (RI; R=CH_3, C_2H_5, or $CH_3CH_2CH_2$) and potassium *t*-butoxide is described, together with the synthesis of α-benzyl ketone of 5β-cholestan-2-one. The bromination of these alkyl derivatives is also described.

Results and Discussion

The reaction of 5β-cholestan-2-one (**1**) with alkyl iodide (RI; R=CH_3, C_2H_5, and $CH_3CH_2CH_2$) and potassium *t*-butoxide yielded the corresponding alkylated ketones (**2a**, **2b**, and **2c**). Each alkylated ketone showed a weak negative Cotton effect in the CD spectrum compared with that of 5β-cholestan-2-one (**1**). Compound **2a** was identical with the hydrogenation product of a hydroxymethylene derivative (**4**), which was obtained by the condensation of 5β-cholestan-2-one with ethyl formate. To determine the position of the hydroxymethylene group in compound **4**, it was brominated with NBS and sodium acetate to yield 3β-bromo-5β-cholestan-2-one.[7] Thus compound **4** was confirmed to be 3-hydroxymethylene-5β-cholestan-2-one.

In order to determine the configuration of **2a** and **2b**, the synthesis of their epimers was attempted. Spencer *et al.*[8] reported that the methylation of the α-bromo ketone with zinc powder–methyl iodide in benzene–dimethyl sulfoxide (10 : 1) in a nitrogen atmosphere gave the α-methyl ketone which retained the configuration at the original site of the bromine. The reaction of 3β-bromo-5β-cholestan-2-one (**5**) with methyl iodide and with ethyl iodide in the presence of zinc powder according to the procedures described above by Spencer *et al.*[8] yielded compounds **6a** and **6b**, respectively. These products (**6a** and **6b**) were isomerized by treatment with concd sulfuric acid in ethanol to give the stable compounds **2a** and **2b**. The structures of the two compounds were confirmed to be 3β-methyl- (**6a**) and 3β-ethyl-5β-cholestan-2-one (**6b**). This was also supported by the CD spectra.

The reaction of 5β-cholestan-2-one (**1**) with benzaldehyde in the presence of base yielded benzylidene ketone (**11**). Hydrogenation of **11** gave a benzyl ketone (**2d**). By comparison with the CD spectra of 3α-alkyl ketones (**2a**, **2b**, and **2c**), the structure of the benzyl ketone (**2d**) was presumed to be 3α-benzyl-5β-cholestan-2-one (**2d**).

The bromination of the alkylated ketones (**2a**, **2b**, **2c**, and **2d**) gave the bromo derivative (**3a**, **3b**, **3c**, or **3d**).

On the basis of the CD, ORD, IR, and NMR spectral data for **3a**, **3b**, **3c**, and **3d**, the structures of these bromo derivatives were determined to be 3α-bromo-3α-alkyl-5β-cholestan-2-ones. This received support from the following evidence. The bromo derivatives (**3a**, **3b**, and **3d**) were reduced with sodium borohydride to give the bromohydrins (**7a**, **7b**, and **7d**), which were converted to the bromohydrin acetates (**8a**, **8b**, and **8d**). The NMR spectra of these bromohydrin acetates showed a quartet at δ 4.24 ppm (J=4.5 and 11.5 Hz) assignable to the 2α-H of an axial character. Therefore, **8a**, **8b**, and **8d** were presumed to be 2β-acetoxy-3β-bromo-3α-alkyl-5β-cholestane. By treating these bromohydrins with potassium hydroxide, the corresponding 3α-alkyl ketone (**2a**, **2b**, or **2d**) was obtained. From these results, a hydroxyl group and a bromine atom of the bromohydrins (**7a**, **7b**, and **7d**) were shown to be *cis*; this led to a 3β-bromo-3α-alkyl-2β-hydroxy-5β-cholestane structure for these bromohydrins.

It was found that the enolisation of the alkylated ketones (**2a** and **2b**) with 60% perchloric acid–acetic anhydride occurred in the direction of a carbon atom possessing an alkyl group, as shown by the NMR spectra. The bromination of the enolisation product (**10a**) of one (**2a**) of the alkylated ketones yielded the 3β-bromo-3α-methyl ketone (**3a**).

From these results, it is suggested that the enolisation of the alkylated ketone occurs at the C_2–C_3 position. The bromination of the 3α-alkyl ketone occurs at a carbon atom having an alkyl group, namely, the C_3β-bond, as has been reported for the bromination of the alkylated ketone.[2]

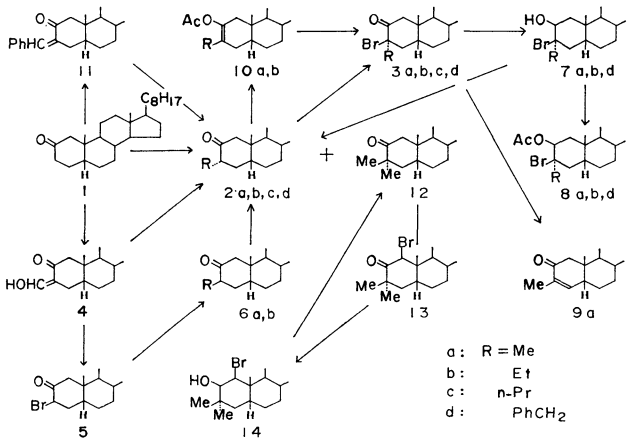
The reaction of 3β-bromo-3α-methyl ketone (**3a**) with lithium chloride gave the α,β-unsaturated ketone (**9a**), which showed absorptions at 1670 and 1632 cm^{-1} in its IR spectrum. It was determined to be 3-methyl-5β-cholest-3-en-2-one (**9a**) by means of its NMR spectrum, which showed a signal at δ 1.72 ppm due to the olefinic methyl proton. Hydrogenation of **9a** in the presence of 10% palladium charcoal gave the 3α-methyl ketone (**2a**). These facts indicate that the direct alkylation of 5β-cholestan-2-one occurs at the C_3 position.

The reaction of 5β-cholestan-2-one (**1**) with excess methyl iodide yielded the dimethylated ketone (**12**) and 3α-methyl ketone (**2a**).

The bromination product of the dimethylated ketone (**12**) was presumed to be 1β-bromo-3,3-dimethyl ketone (**13**) from the sign of the Cotton effect, the Δ[A]-, and the $\Delta\lambda_1$-values [+141 (+11,200) and +24 nm, as compared with the corresponding values for the dimethylated ketone (**12**)] in the ORD (CD) spectrum, the shift of the C=O stretching band (1703 cm^{-1}) in the IR spectrum, and from the signal (δ 4.29 ppm, singlet) due to the C_1HBr in the NMR spectrum. From these spectral data, it can be considered that the conformation in the A ring of **13** is a distorted form due to the 1 : 3-interaction between the C_1β–Br bond and the C_3β–Me bond.

The bromo ketone (**13**) was then converted to the dimethylated bromohydrin (**14**) by reduction with sodium borohydride, as described above. By treatment of **14** with potassium hydroxide in 2-propanol under reflexing conditions, the dimethylated ketone (**12**) was obtained. From these results, the dimethylated bromohydrin (**14**) was identified as 1β-bromo-2β-hydroxy-3,3-dimethyl-5β-cholestane.

Thus, on the basis of all of the foregoing results, it was concluded that the α-alkylation and the aldol condensation of 5β-cholestan-2-one (**1**) occur at the C_3 position, in contrast with the case of the enolisation and the halogenation of 5β-cholestan-2-one (**1**). It was further concluded that the enolisation of the alkylated ketone occurs in the direction of C_3, and that the bromination of these alkylated ketones forms the 3β-bromo-3α-alkyl ketones.



Experimental

All the melting points are uncorrected. The IR, ORD, and CD spectra were measured using a Hitachi model 215 grating infrared spectrophotometer and a model J-20 spectropolarimeter. The NMR spectra were measured in carbon tetrachloride, with TMS as the internal standard, using a nuclear magnetic resonance spectrometer, Hitachi-Perkin Elmer R-20A.

*3α-Methyl-5β-cholestan-2-one (**2a**)* A mixture of **1** (500 mg), methyl iodide (1.0 ml), and potassium *t*-butoxide (200 mg) in *t*-butyl alcohol–dry benzene (1 : 1) (10 ml) was refluxed under stirring in a nitrogen atmosphere for 2 h. The reaction was then removed under reduced pressure; the residue was poured into water and extracted with ether. The ethereal solution was washed with water, dried, and evaporated under reduced pressure. The resultant oil (510 mg) was chromatographed on silica gel (20 g). Elution with benzene–petroleum ether (1:5) (540 ml) gave plates of **2a** (55 mg), from methanol–acetone, mp 102.5—105.5 °C, IR (KBr): 1706 cm^{-1}; ORD (*c*, 0.980, Di) at 27 °C: $[\alpha]_D$ +36.7°, $[\alpha]_{400}$ +78.1°, $[\alpha]_{324}$ 0°, $[\alpha]_{316}$ −99.3° (trough), $[\alpha]_{311}$ 0°, $[\alpha]_{306}$ +49.0° (shoulder), $[\alpha]_{283}$ +410.7° (peak); CD (*c*, 0.980, Di) at 27 °C: $[\theta]_{311}$ −850° (shoulder), $[\theta]_{302}$ −1218° (trough), and $[\theta]_{294}$ −1019° (shoulder).

Found: C, 84.11; H, 11.84%. Calcd for $C_{28}H_{48}O$: C, 83.93; H, 12.08%.

The next fraction, eluted by the same solvent (360 ml) on crystallization from ethanol, gave plates of **1** (95 mg), mp 82—84.5 °C.

*3α-Ethyl-5β-cholestan-2-one (**2b**).* A mixture of **1** (3.0 g), potassium *t*-butoxide (3.02 g), and ethyl iodide (4.0 ml) in *t*-butyl alcohol–benzene was treated according to the procedure described for the methylation of **1**. After the usual work-up, the resultant oil was chromatographed on silica gel (100 g). Elution with hexane (800 ml) and hexane–benzene (10 : 1) (500 ml) gave plates of **2b** (601 mg) from ethanol, mp 92—93 °C, IR (KBr): 1706 cm^{-1}; ORD (*c*, 0.066, Di) at 20 °C: $[\alpha]_D$ +24.2°, $[\alpha]_{400}$ +54.5°, $[\alpha]_{335}$ +60.6°, $[\alpha]_{320}$ +24.2° (trough), and $[\alpha]_{292}$ +29.4° (peak); CD (*c*, 0.567, Di) at 19 °C: $[\theta]_{312}$ −453.6°, $[\theta]_{309}$ −434.3° (shoulder), $[\theta]_{304}$ −499.4° (trough), and $[\theta]_{275}$ +168.9° (peak).

Found: C, 84.14; H, 12.32%. Calcd for $C_{29}H_{50}O$: C, 83.99; H, 12.15%.

*3α-Propyl-5β-cholestan-2-one (**2c**).* A mixture of **1** (4.0 g), potassium *t*-butoxide (4.0 g), and propyl iodide (6.0 ml) in *t*-butyl alcohol–benzene (1 : 1) was treated according to the procedure described for the methylation of **1**. After the usual work-up, the resultant oil (4.1 g) was chromatographed on silica gel (100 g). Elution with hexane (1200 ml) gave plates of **2c** (282 mg) from ethanol–acetone, mp 74—74.5 °C, IR (KBr): 1706 cm^{-1}; ORD (*c*, 0.171, Di) at 21 °C: $[\alpha]_D$ +35.2°, $[\alpha]_{400}$ +117.3°, $[\alpha]_{328}$ +105.6° (trough), and $[\alpha]_{292}$ +263.9° (peak); CD (*c*, 0.572, Di) at 19 °C: $[\theta]_{310}$ −341.5°, $[\theta]_{303}$ −353.9° (trough), and $[\theta]_{273}$ +163.3° (peak).

Found: C, 84.34; H, 12.41%. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.23%.

The next fraction was eluted with benzene (800 ml) and on crystallization from ethanol gave 5β-cholestan-2-one (**1**) (1.472 g), mp 86—88 °C.

*3-Hydroxymethylene-5β-cholestan-2-one (**4**).* The ketone (**1**) (753 mg) in dry benzene (10 ml) was treated with ethyl formate (763 mg) and sodium methoxide (131 mg) in a nitrogen atmosphere for 4 h at room temperature. The reaction mixture was then taken up in ether, and the ether extracts were washed with dilute hydrogen chloride and water, dried, and evaporated. The crystallization of the residue from methanol–ether gave plates of **4** (531 mg), mp 128—130 °C, IR (KBr): 1646 and 1593 cm^{-1}; UV (EtOH) λ_{max} 281 nm: (log 4.13).

Found: C, 80.88; H, 11.54%. Calcd for $C_{28}H_{46}O_2$: C, 81.10; H, 11.18%.

*3β-Methyl-5β-cholestan-2-one (**6a**).* The bromo ketone (**5**) (200 mg) in benzene–dimethyl sulfoxide (10 : 1) (11 ml) was stirred with zinc powder (500 mg) and methyl iodide (2.5 ml) in a nitrogen atmosphere at 40—45 °C for 4 h. After the usual work-up, the resultant oil (144 mg) was chromatographed on silica gel (30 g). Elution with hexane (100 ml) gave needles of **6a** (19 mg) from ethanol, mp 120—121 °C, IR (KBr): 1708 cm^{-1}; ORD (*c*, 0.6815, Di) at 22 °C: $[\alpha]_D$ −1.47°, $[\alpha]_{400}$ −5.87°, $[\alpha]_{320}$ −89.5° (trough), $[\alpha]_{312}$ −55.8°

(peak), $[\alpha]_{310}$ −60.2° (trough), and $[\alpha]_{274}$ +105.6° (peak); CD (*c*, 0.6815, Di) at 22 °C: $[\theta]_{316}$ −346.9° (shoulder), $[\theta]_{305}$ −570.3° (trough), $[\theta]_{301}$ −517.4° (peak), and $[\theta]_{296}$ −558.6° (trough).

Found: *m/e* 400.3718. Calcd for $C_{28}H_{48}O$: M, 400.6866.

The next fraction was eluted with hexane–benzene (1 : 1) (150 ml) and on crystallization from ethanol gave 5β-cholestan-2-one (**1**) (52 mg), mp 85—88 °C.

*3β-Ethyl-5β-cholestan-2-one (**6b**).* A mixture of **5** (320 mg), zinc powder (800 mg), and ethyl iodide (4.0 ml) in benzene–dimethyl sulfoxide (10 : 1) (17.6 ml) was treated according to the procedure described for the methylation of **5**. After the usual work-up, the resultant oil (295 mg) was chromatographed on silica gel (20 g). Elution with hexane–benzene (1 : 1) (250 ml) gave needles of **6b** (5 mg) from ethanol, mp 107—108 °C, IR (KBr): 1700 cm^{-1}; ORD (*c*, 0.336, Di) at 24 °C; $[\alpha]_D$ +68.4°, $[\alpha]_{400}$ +181.3°, $[\alpha]_{319}$ +633.2° (peak), $[\alpha]_{314}$ +591.6° (trough), $[\alpha]_{308}$ +633.2° (peak), $[\alpha]_{299}$ +401.3° (shoulder), and $[\alpha]_{273}$ +11.89° (trough); CD (*c*, 0.336, Di) at 24 °C: $[\theta]_{315}$ +1158.9° (shoulder), $[\theta]_{304}$ +2305.4° (peak), $[\theta]_{300}$ +2256.1° (trough), $[\theta]_{294}$ +2551.9° (peak), and $[\theta]_{287}$ +2157° (shoulder).

Found: *m/e* 414.3850. Calcd for $C_{29}H_{50}O$: M, 414.7134.

The next fraction was eluted with the same solvent (150 ml) and on crystallization from ethanol gave 5β-cholestan-2-one (**1**) (119 mg), mp 83—86 °C.

*Isomerization of 3β-Methyl- (**6a**) and 3β-Ethyl-5β-cholestan-2-one (**6b**).* 3β-Methyl (**6a**) and 3β-ethyl ketone (**6b**) (12 mg) in ethanol (10 ml) was treated with a few drops of concd sulfuric acid under refluxing for 2 h. After the usual work-up, crystallization from ethanol afforded plates of **2a** (7 mg) (mp 101—105 °C) and **2b** (5 mg) (mp 89—92 °C), respectively.

*Hydrogenation of 3-Hydroxymethylene-5β-cholestan-2-one (**4**).* The hydroxymethylene ketone (**4**) (200 mg) was hydrogenated in the usual method over 10% palladium charcoal in ethanol–ether (4 : 1) (25 ml). After the usual work-up, crystallization from ethanol afforded plates of **2a** (97 mg), mp 101—103 °C.

*3β-Bromo-5β-cholestan-2-one (**5**).* A mixture of **4** (100 mg), sodium acetate (132 mg) in acetic acid (0.12 ml), and *N*-bromosuccinimide (44.6 mg) in dioxane–water (10 : 1) (11 ml) was stirred overnight at room temperature. After the usual work-up, crystallization of the residue from ethanol gave plates of **5** (67 mg), mp 139—142 °C.

*3β-Bromo-3α-methyl-5β-cholestan-2-one (**3a**).* The methylated ketone (**2a**) (500 mg) in acetic acid (20 ml) was treated with bromine (219 mg) in acetic acid (1.5 ml) containing a few drops of 48% hydrobromic acid at room temperature for 15 min. The reaction mixture was taken up in ether, and the ethereal extracts were washed with a sodium hydrogencarbonate solution and water, dried, and evaporated. The crystallization of the residue from ethanol gave needles of **3a** (364 mg), mp 126—128 °C, IR (KBr): 1712 cm^{-1}; ORD (*c*, 0.794, Di) at 24 °C: $[\alpha]_D$ −94.4°, $[\alpha]_{400}$ −582.4°, $[\alpha]_{337}$ +3085° (trough), and $[\alpha]_{290}$ +3728° (peak); CD (*c*, 0.794, Di) at 24 °C: $[\theta]_{314}$ −25710° (trough).

Found: C, 69.47; H, 9.56%. Calcd for $C_{28}H_{47}OBr$: C, 70.11; H, 9.88%.

*3β-Bromo-3α-ethyl-5β-cholestan-2-one (**3b**).* The bromination of **2b** (50 mg) was carried out using the technique described for the synthesis of 3β-bromo-3α-methyl-5β-cholestan-2-one. After the usual work-up, the resultant oil, on crystallization from methanol, gave needles of **3b** (25 mg), mp 85—86 °C, IR (KBr): 1709 cm^{-1}; ORD (*c*, 0.220, Di) at 22 °C: $[\alpha]_D$ −43.1°, $[\alpha]_{400}$ −272.3°, $[\alpha]_{339}$ −1234° (trough), and $[\alpha]_{290}$ +1688° (peak); CD (*c*, 0.220, Di) at 22 °C: $[\theta]_{318}$ −11469° (trough) and $[\theta]_{290}$ +1688° (peak).

Found: C, 70.12; H, 10.33%. Calcd for $C_{29}H_{49}OBr$: C, 70.57; H, 10.01%.

*3β-Bromo-3α-propyl-5β-cholestan-2-one (**3c**).* The bromination of **2c** (290 mg) was carried out using the technique described for the synthesis of 3β-bromo-3α-methyl-5β-cholestan-2-one. After the usual work-up, the resultant oil, on crystallization from methanol–acetone, gave needles of **3c** (136 mg), mp 83—84 °C, IR (KBr): 1709 cm^{-1}; ORD (*c*, 0.287, Di) at 23 °C: $[\alpha]_D$ −65.4°, $[\alpha]_{400}$ −505.8°, $[\alpha]_{338}$ −2591.6° (trough), $[\alpha]_{318}$ 0°, and $[\alpha]_{289}$ +3261° (peak); CD (*c*, 0.287, Di) at 23 °C: $[\theta]_{318}$ −22753° (trough).

Found: C, 71.06; H, 10.21%. Calcd for $C_{30}H_{51}OBr$: C, 70.98; H, 10.13%.

*3-Benzylidene-5β-cholestan-2-one (**11**).* The ketone (**1**) (256 mg) in methanol (50 ml) was refluxed under stirring with benzaldehyde (7.8 ml) and sodium hydroxide (1.4 g) for 2.5 h. The reaction mixture was then removed under reduced pressure; the residue was poured into water, and extracted with ether. The ethereal solution was washed with sodium bisulfite solution and water, dried, and evaporated. The crystallization of the residue from methanol gave plates of **11** (270 mg), mp 140—141 °C, IR (KBr): 1675, 1587, and 1569 cm^{-1}.

Found: C, 86.04; H, 10.90%, Calcd for $C_{34}H_{50}O$: C, 86.02; H, 10.61%.

*3α-Benzyl-5β-cholestan-2-one (**2d**).* The benzylidene ketone (**11**) (2.10 g) was hydrogenated in the usual way over 10% palladium charcoal in ethanol–ether (10 : 1) (150 ml). After 4 h, the filtrate from catalyst was evaporated under reduced pressure. The crystallization of the residue from ethanol gave needles of **2d** (1.751 g), mp 134—135 °C, IR (KBr): 1709 and 1600 cm^{-1}; ORD (*c*, 0.381, Di) at 22 °C: $[\alpha]_D$ +99.7°, $[\alpha]_{400}$ +251.9°, $[\alpha]_{316}$ +426.4° (trough), and $[\alpha]_{284}$ +911.8° (peak); CD (*c*, 0.238, Di) at 21 °C: $[\theta]_{312}$ −800.7° (trough), $[\theta]_{308}$ −688.1° (peak), and $[\theta]_{303}$ −738.1° (trough).

Found: C, 85.96; H, 11.12%. Calcd for $C_{34}H_{52}O$: C, 85.65; H, 10.99%.

*3β-Bromo-3α-benzyl-5β-cholestan-2-one (**3d**).* A mixture of **2d** (959 mg), bromine (354 mg) in acetic acid (3.1 ml) containing a few drops of 48% hydrobromic acid, and acetic acid (40 ml) was allowed to react according to the procedure described for the synthesis of the 3β-bromo-3α-methyl ketone. After the usual work-up, the resultant oil, on crystallization from ethanol, gave needles of **3d** (604 mg), mp 109—111 °C, IR (KBr): 1712 cm^{-1}; ORD (*c*, 0.333, Di) at 22 °C: $[\alpha]_D$ +21.0°, $[\alpha]_{460}$ 0°, $[\alpha]_{400}$ −24.0°, $[\alpha]_{238}$ −1005.7° (trough), $[\alpha]_{321}$ 0°, and $[\alpha]_{290}$ +2176.5° (peak); CD (*c*, 0.333, Di) at 22 °C: $[\theta]_{318}$ −13212° (trough).

Found: C, 73.61; H, 9.30%. Calcd for $C_{34}H_{51}OBr$: C, 73.49; H, 9.25%.

*3-Methyl-5β-cholest-3-en-2-one (**9a**).* A mixture of **3a** (115 mg), lithium chloride (250 mg), and *N*,*N*-dimethylformamide (10 ml) was refluxed under stirring for 40 min. The reaction mixture was then taken up in ether, and the ether extracts were washed with dilute hydrochloric acid and water, dried, and evaporated. The crystallization of the residue from methanol–ether gave plates of **9a** (55 mg), mp 114—115.5 °C, IR (KBr): 1670 cm^{-1}; NMR (CCl_4) δ=6.18 (1H, m) and 1.72 (3H, m); ORD (*c*, 0.346, Di) at 30 °C: $[\alpha]_D$ −15.9°, $[\alpha]_{400}$ −216.8°, $[\alpha]_{373}$ −439.4° (trough), $[\alpha]_{367}$ −427.9° (peak), $[\alpha]_{358}$ −508.8° (trough), $[\alpha]_{346}$ −263.1° (peak), $[\alpha]_{343}$ −268.9° (trough), $[\alpha]_{335}$ 0°, $[\alpha]_{331}$ +57.8° (peak), $[\alpha]_{329}$ +52.0° (trough), $[\alpha]_{320}$ +196.6° (peak), $[\alpha]_{315}$ +161.9° (trough), $[\alpha]_{311}$ +170.6° (peak), $[\alpha]_{296}$ 0°, $[\alpha]_{255}$ −2205.9° (trough), $[\alpha]_{242}$ 0°, and $[\alpha]_{222}$ +5392.2° (peak); CD (*c*, 0.346,

Di) at 30 °C: $[\theta]_{347}$ −2091° (trough), $[\theta]_{342}$ −2054° (peak), $[\theta]_{335}$ −2529° (trough), $[\theta]_{328}$ −2054° (shoulder), $[\theta]_{280}$ −209.2° (peak), $[\theta]_{241}$ −14182° (trough), $[\theta]_{224}$ 0°, and $[\theta]_{214}$ +60168° (peak).

Found: C, 84.18; H, 11.86%. Calcd for $C_{28}H_{46}O$: C, 84.35; H, 11.63%.

*Hydrogenation of 3-Methyl-5β-cholest-3-en-2-one (**9a**).* A mixture of **9a** (50 mg), 10% palladium charcoal, and hydrogen in ethanol was treated according to the procedure described for the hydrogenation of **4**. After the usual work-up, the resultant oil, on crystallization from ethanol, gave plates of **2a** (19 mg), mp 101—103 °C.

*3,3-Dimethyl-5β-cholestan-2-one (**12**).* The ketone (**1**) (1.0 g) in *t*-butyl alcohol-dry benzene (1 : 1) (25 ml) was treated with methyl iodide (11.0 ml) and potassium *t*-butoxide (3.0 g) under refluxing in a nitrogen atmosphere for 6 h. After the usual work-up, the resultant oil (1.065 g) was chromatographed on silica gel (100 g). Elution with benzene-petroleum ether (1 : 5) (720 ml) gave plates of **12** (365 mg) from acetone, mp 100—101.5 °C, IR (KBr): 1706 cm^{-1}, ORD (*c*, 1.132, Di) at 22 °C: $[\alpha]_D$ +1.77°, $[\alpha]_{400}$ −53.5°, $[\alpha]_{319}$ −954.4° (trough), $[\alpha]_{311}$ −600.9° (peak), $[\alpha]_{309}$ −636.3° (trough), $[\alpha]_{303}$ 0°, and $[\alpha]_{275}$ +1113.4° (peak); CD (*c*, 1.132, Di) at 22 °C: $[\theta]_{313}$ −3870° (shoulder), $[\theta]_{303}$ −6289° (trough), $[\theta]_{298}$ −6047° (peak), and $[\theta]_{294}$ −6168° (trough).

Found: C, 84.53; H, 12.17%. Calcd for $C_{29}H_{50}O$: C, 83.99; H, 12.15%.

The next fraction, eluted with the same solvent (570 ml), on crystallization from methanol-acetone gave 3α-methyl-5β-cholestan-2-one (**2a**) (147 mg), mp 97—104 °C.

*1β-Bromo-3,3-dimethyl-5β-cholestan-2-one (**13**).* The bromination of **12** (300 mg) was carried out using the technique described for the synthesis of **3a**. After the usual work-up, the resultant oil, on crystallization from acetone, gave needles of **13** (200 mg), mp 138—141 °C, IR (KBr): 1703 cm^{-1}; NMR (CCl_4) δ=4.29 (1H, s); ORD (*c*, 0.365, Di) at 30 °C: $[\alpha]_D$ +30.1°, $[\alpha]_{400}$ +123.2°, $[\alpha]_{343}$ +533.8° (peak), $[\alpha]_{320}$ 0°, and $[\alpha]_{280}$ −588.5° (trough); CD (*c*, 0.365, Di) at 30 °C: $[\theta]_{321}$ +4906° (peak), $[\theta]_{317}$ +3746° (trough), $[\theta]_{312}$ +3836° (peak), and $[\theta]_{230}$ −3479° (trough).

Found: C, 70.38; H, 10.27%. Calcd for $C_{29}H_{49}OBr$: C, 70.57; H, 10.01%.

*The Enolisation of 3α-Methyl-5β-cholestan-2-one (**2a**).* This enolisation was treated according to the method of the enolisation described for 5β-cholestan-2-one.[7] The reaction product gave plates of 2-acetoxy-3-methyl-5β-cholest-2-ene (**10a**) from ethanol, mp 78—79 °C, IR (KBr): 1750 and 1739 cm^{-1}; NMR ($CDCl_3$) δ=2.11 (3H, s). A mixture of **10a** (20 mg), bromine (7.9 mg) in tetrachloromethane, and tetrachloromethane (10 ml) containing a few drops of epichlorohydrin was carried out according to the directions of Djerassi *et al.* described for 2-acetoxy-5α-cholest-2-ene.[9] After the usual work-up, the resultant oil, on crystallization from ethanol, gave needles of **3a** (15 mg), mp 126—128 °C.

*Confirmation of the Configuration of 3β-Bromo-3α-methyl-5β-cholestan-2-one (**3a**) by Using Chemical Reactions.* The bromo derivative (**3a**) (60 mg) in methanol-ether (1 : 2) (15 ml) was treated with sodium borohydride (20 mg) at room temperature. After 45 min, water was added and the mixture was extracted with ether. The ethereal solution was washed with water, dried, and evaporated under reduced pressure. Attempts to crystallize the resultant oil (**7a**) were unsuccessful, and the product was used for the next step without purification [IR (NaCl): 3444 cm^{-1}]. A mixture of the methyl bromohydrin (**7a**) (15 mg), acetic anhydride (3 ml), and pyridine (3 ml) was allowed to stand at room temperature overnight. After the usual work-up, attempts to crystallize the resultant oil (**8a**) were unsuccessful. The methylated bromohydrin (**7a**) (35 mg) in 2-propanol (5 ml) was treated with a solution of potassium hydroxide (20 mg) in the same solvent (3 ml), and the mixture was refluxed for 30 min. 2-Propanol was then removed under reduced pressure; the residue was diluted with water, and extracted with ether. The ethereal solution was washed with water, dried, and evaporated under reduced pressure. Crystallization of the residue from methanol gave plates of **2a** (13 mg), mp 101—104 °C.

*Confirmation of the Configuration of 1β-Bromo-3,3-dimethyl-5β-cholestan-2-one (**13**) by Using Chemical Reactions.* The dimethylated bromo ketone (**13**) (150 mg) in methanol-ether (1 : 2) (30 ml) was treated with sodium borohydride (50 mg) at room temperature. After the usual work-up, the resultant oil, on crystallization from ethanol-ether, gave needles of dimethylated bromohydrin (**14**) (97 mg), mp 118—119 °C, IR (KBr): 3575 cm^{-1}; NMR (CCl_4) δ=4.75 (1H, d, J=3.6 Hz). A mixture of **14** (57 mg) and potassium hydroxide (46 mg) in 2-propanol (10 ml) was allowed to react according to the procedure described for the synthesis of 3α-methyl ketone (**2a**) from 3-methyl bromohydrin (**7a**). After the usual work-up, the resultant oil, on crystallization from acetone, gave plates of **12** (17 mg), mp 100—101.5 °C.

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