SOLVOLYSIS OF 5,6β-CYCLOPROPANO-5β-CHOLESTANE-3β,19-DIOL 3-ACETATE 19-*p*-TOLUENESULPHONATE*

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Acetolysis of 5,6β-cyclopropano-5β-cholestane-3β,19-diol 3-acetate 19-*p*-toluenesulphonate afforded 5,6β-cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-ene-3β-ol 3-acetate and 7β,19-cyclo-B-homo-5α-cholestane-3β,5-diol 3,5-diacetate. The structures of these products were established by spectral and chemical means.

In our previous paper[1] we delt with Simmons–Smith methylenation of the 5,6-unsaturated 19-hydroxylated steroids and described the synthesis of the 5β,6β-cyclopropano derivative *I*. In this paper we described the acetolysis as well as some other reactions of the tosylate *II* and the mesylate *III* which led to novel products with a modified steroid skeleton.

When the tosylate *II* was submitted to acetolytic conditions (acetic acid–potassium acetate) two new products were formed in about equal quantities. One of them still contained the cyclopropane ring and, in addition, a double bond; the second product was a saturated diol-diacetate with one tertiary acetoxy group. The unsaturated compound was also obtained as the sole product from the tosylate *II* with sodium iodide in 1,2-dimethoxyethane, by treatment over silica gel or, from the mesylate *III* with lithium aluminium hydride. Structures of these compounds were established by spectral as well as by chemical means.

^{1}H-NMR spectrum of the unsaturated compound showed presence of the cyclopropane ring, of a trisubstituted double bond (one olefinic proton, triplet at 5·29 ppm) and AcO—CH—CH_2—C=C< grouping. Hydrolysis afforded the alcohol *IV* which was oxidized by Jones' reagent to the β,γ-unsaturated ketone *VI*. This ketone showed a pronounced negative Cotton effect on CD ($\Delta\varepsilon_{300}$ −14·52) which is due to the presence of the double bond as the saturated ketones *XIX* and *XXIV* exhibited very low ($\Delta\varepsilon_{293}$ +0·33 and $\Delta\varepsilon_{290}$ −2·00, respectively) Cotton effects. The octant projection of the ketone *VI* in the supposed conformation is presented in Fig. 1. Hydride reduc-

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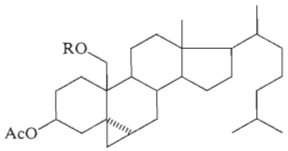
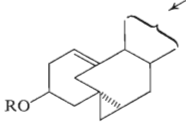
tion of the ketone *VI* yielded the 3α-hydroxy derivative *VII* which was oxidized back to the starting ketone *VI*.

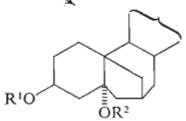
When submitted to catalytic hydrogenation (Adams' catalyst in acetic acid) the olefin *IV* afforded the saturated cyclopropano derivative *XV*. Under prolonged treatment cleavage of the cyclopropane ring took place giving rise to the 5β-methyl derivative *XVII* the structure of which follows from the ^{1}H-NMR spectrum (singlet at 0·91 ppm for the 5β-methyl group). The 10α-configuration was assigned tentatively.



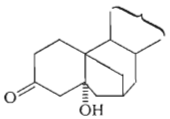
I, R = H
II, R = Tos
III, R = Mes



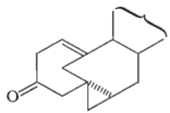
IV, R = H
V, R = Ac



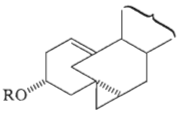
IX, $R^1 = R^2 = H$
X, R^1 = Ac, R^2 = H
XI, $R^1 = R^2$ = Ac



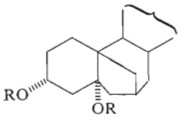
XII



VI



VII, R = H
VIII, R = Ac



XIII, R = H
XIV, R = Ac

Similarly, the 3α-hydroxy derivative *VII* afforded under analogous conditions the saturated derivatives *XX* and *XXII*. These alcohols were characterized also as the acetates *XVI*, *XVIII*, *XXI*, and *XXIII*. Oxidation of the alcohols *XV* and *XX* yielded the ketone *XIX*, similar treatment of the alcohols *XVII* and *XXII* gave the ketone *XXIV*.

To get additional information about this reaction and its product we carried out the solvolysis with the tosylate *XXVIII* carrying two deuterium atoms at $C_{(19)}$. This compound was prepared from the 19-hydroxy derivative *I* by oxidation to the corresponding acid followed by esterification to the methyl ester *XXV*. Reduction with lithium aluminium deuteride afforded the diol *XXVI* which was selectively acetylated to the monoacetate *XXVII* and subsequently esterified to the 19-tosylate *XXVIII*. Reaction with sodium iodide in 1,2-dimethoxyethane afforded the desired labelled product *XXX* with the two deuterium atoms incorporated in the molecule as confirmed by mass spectrometry. The ^{1}H-NMR spectrum was identical in all details with the spectrum of the unlabelled product *V* showing that neither the olefinic proton nor the cyclopropane protons originated from the $C_{(19)}$ hydrogens and we may conclude that in this compound the cyclopropane ring remained untouched during the reaction. For mass spectrometric studies we also prepared the labelled derivatives *XXIX*, *XXXI*, and *XXXII*.

Further valuable evidence supporting the structure *V* was provided by mass spectrometry: The mass spectrum of the acetate *V* exhibits molecular ions $C_{30}H_{48}O_2^{+\cdot}$, m/z 440 indicating that the product was formed from the tosylate *II* by a formal loss of *p*-toluenesulphonic acid. The $(M - CH_3COOH)^{+\cdot}$ ions decompose futher by losing C_2H_4, C_2H_5, C_3H_5, C_3H_6, C_4H_8, C_5H_9, C_7H_{10}, C_8H_{17}, $C_{10}H_{13}$, $C_{10}H_{19}$, $C_{10}H_{20}$, $C_{10}H_{21}$, and $C_{11}H_{23}$ neutral fragments. The mass spectrum of the labelled derivative *XXX* shows that both deuterium atoms are cleanly preserved in the molecular ion

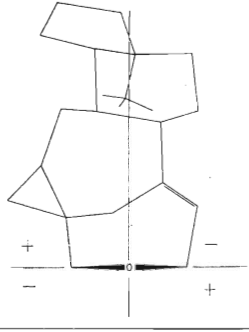
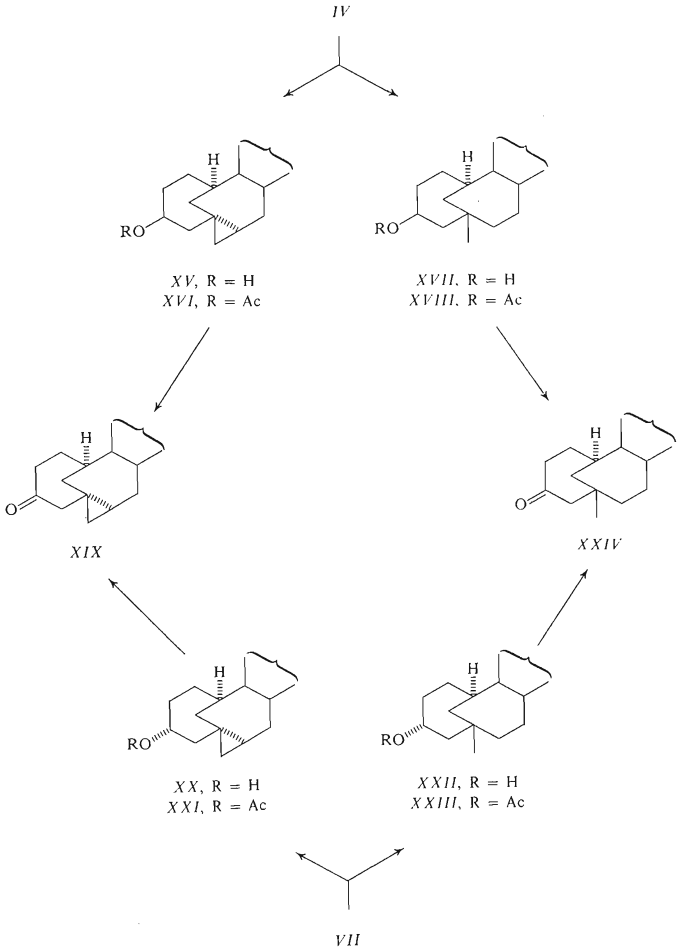
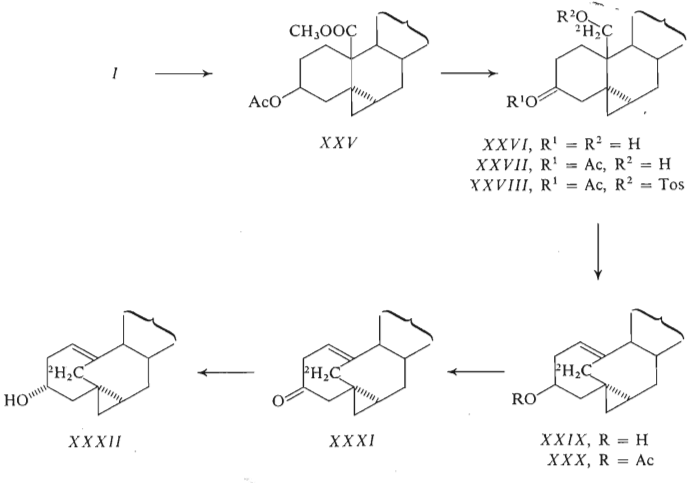


FIG. 1
Octant Projection of the Unsaturated Ketone *VI*


IV
H
RO
XV, R = H
XVI, R = Ac
XVII, R = H
XVIII, R = Ac
O
XIX
XXIV
XX, R = H
XXI, R = Ac
XXII, R = H
XXIII, R = Ac
VII

(96·5% of the $^2H_2$-species) and in all significant ions except for $(M-CH_3COOH-C_4H_8)^{+\cdot}$, $(M-CH_3COOH-C_7H_{10})^{+\cdot}$, and $(M-CH_3COOH-C_{10}H_{13})^{+\cdot}$. The mass spectrum of the ketone *VI* contains significant ions due to the loss of CH_2. $COCH_3$, CH_3COCH_3, C_5H_7O, C_7H_9O, and $C_{10}H_{13}O$ neutral fragments. Hence, the C and D rings in the compounds *V*, *VI*, and *XXX* remained intact during the rearrangement.

Molecular ions of the hydrogenated ketone *XXIV* ($C_{28}H_{48}O^{+\cdot}$, *m/z* 400) decompose by losing CO, C_3H_6O, C_4H_8O, $C_5H_{10}O$, $C_6H_{10}O$, and $C_8H_{13}O$ neutral fragments. The abundant $(M-C_3H_6O)^{+\cdot}$ ions are evidence that the ketone *XXIV*, contains a $-CH_2-CO-CH_2-\underset{\displaystyle C}{\overset{\displaystyle C}{\underset{|}{\overset{|}{C}}}}-CH_3$ subunit[2,3]. The loss of C_7H_9O and $C_8H_{13}O$ from compounds *III* and *V*, respectively, indicates the presence of a seven-membered ring in our compound. In order to support the suggested structure we made use of the well known stereospecificity of the electron-impact-induced water elimination[4]. As shown in Fig. 2 the 3β-hydroxyl in structure *V* may approach closely to the hydrogens at 5(10) a position (supposed to represent originally the $C_{(19)}$ group), such situation being in none of the other structures compatible with our spectral data. As expected, H^2HO is lost cleanly from the molecular ions of the labelled alcohol *XXIX*



whereas the mass spectrum of the epimeric labelled alcohol *XXXII* shows the loss of H_2O only. We therefore suggest the structure *V* for the unsaturated product of acetolysis.

Further, we turned out attention to the saturated product *XI*. Spectral data showed absence of the cyclopropane ring and a double bond as well. Hydrogenation and epoxidation experiments proved the spectral evidence. In addition, the product contained a tertiary acetoxy group as was shown by spectral and chemical means. Hydrolysis of the diacetate *XI* afforded the diol *IX* which was acetylated to the monoacetate *X* and oxidized to the ketol *XII*, respectively. Hydride reduction of this ketol yielded the diol *XIII* as the only product; its oxidation afforded back the starting ketol *XII*. In the alcohols *IX* and *XIII* the A ring adopts a boat conformation in which both protons at $C_{(3)}$ have pseudoaxial conformation (Fig. 3) as follows from spectra

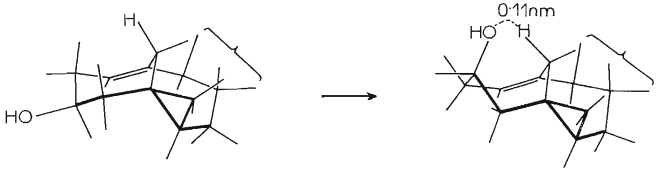


FIG. 2
Conformations of the Ring A in the Alcohol *V*

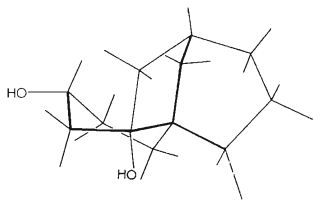
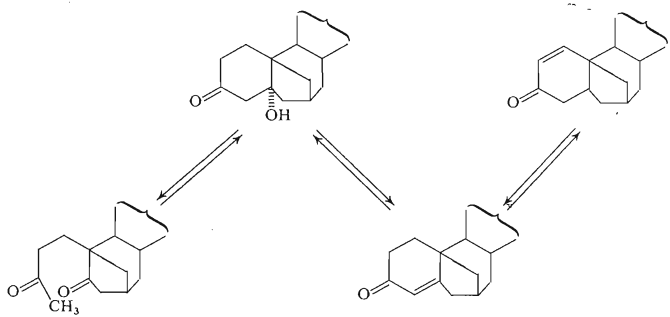


FIG. 3
Boat Conformation of the Ring A in the Alcohols *IX* and *XIII*

data: In the 3β-alcohol *IX* the 3α-proton shows $W_{1/2}$ = 28 Hz and in the epimer *XIII* the half width for the 3β-proton is 23 Hz. In accordance, the diol *XIII* showed no hydrogen bonding in IR. Mass spectrum of the diacetate *XI* showed molecular peak of low intensity *m/z* 500 and abundant ions $(M-CH_3COOH)^{+\bullet}$, *m/z* 440, $(M-2\,CH_3COOH)^{+\bullet}$, *m/z* 380 and $C_9H_{11}^+$, *m/z* 119. The diol *IX* gives abundant molecular ions $(C_{28}H_{48}O_2^{+\bullet})$ which lose easily a C_4H_9O fragment giving rise to $C_{24}H_{39}O^{+\bullet}$ ions, *m/z* 343. The C_9 fragment which is also abundant in the diol *IX* corresponds to $C_9H_{14}O_2^{+\bullet}$, *m/z* 154. The hydroxy ketone *XII* behaves similarly providing abundant ions $C_{28}H_{46}O_2^{+\bullet}$ $(M^{+\bullet})$, $C_{24}H_{39}O^+$ $(M-C_4H_7O)^+$ and $C_9H_{12}O_2^{+\bullet}$. Two possible structures may be deduced for the skeleton of our product: *i.e.* the suggested structure *IX* and an alternative structure with the six-membered ring B and a two-carbon bridge from $C_{(10)}$ to $C_{(6)}$. The two structures were distinguished by a labelling experiment: The deuteration of the hydroxy ketone *XII* with a large excess of deuterium oxide resulted in incorporation of nine deuterium atoms. Comparing the two structures in question only that with the seven-membered ring B is expected to exchange 9 deuterium atoms (hydrogens at $C_{(1)}$, $C_{(2)}$, $C_{(4)}$, $C_{(6)}$, and $C_{(5)}$—OH) by the retroaldol-aldol and dehydration–hydration mechanism shown in Scheme 1. In the alternative structure with the six-membered B-ring we may expect only 7 hydrogens to be exchanged. We therefore suggest structure *XI* for the saturated product of acetolysis of the tosylate *II*.



SCHEME 1

EXPERIMENTAL

Melting points were determined on a Kofler block. Optical measurements were carried out in chloroform with an error of ±2°. The infrared spectra were recorded on the Zeiss UR 20 spectrometer in tetrachloromethane. The ^{1}H-NMR spectra were recorded on the Varian HA-100

instrument in deuteriochloroform and corrected to tetramethylsilane (7·25 ppm). The chemical shift is given in ppm. The CD spectra were recorded on a Dichrographe II (Jouan–Roussel) in methanol. Mass spectra were recorded on a JEOL JMS D-100 spectrometer, operating at 14 to 75 eV. The samples were introduced by means of a direct inlet at lowest temperatures enabling evaporation. Elemental compositions of all discussed ions were measured by peak matching. Decompositions of metastable ions in the first field-free region were measured by accelerating voltage scan method. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin-layer chromatography (TLC) and by spectral evidence. Usual working up of a solution implies washing the solution with 5% aqueous hydrochloric acid, water, drying over sodium sulphate, and evaporation of the solvent under reduced pressure.

5,6β-Cyclopropano-5β-cholestane-3β,19-diol 3-Acetate 19-*p*-Toluenesulphonate (*II*)

The alcohol[1] *I* (5 g) in pyridine (40 ml) was treated with *p*-toluenesulphonyl chloride (5 g) and allowed to stand at room temperature for 18 h. The excess chloride was decomposed with ice and water, and the oily product was taken into ether. The ethereal solution was worked up and the residue after evaporation of the solvent was crystallized from methanol–ether to yield 4·2 g of the tosylate *II*, m.p. 145—146°C, $[\alpha]_D^{20}$ —18° (*c* 1·15). For $C_{37}H_{56}O_5S$ (612·9) calculated: 72·50% C, 9·21% H, 5·23% S; found: 72·13% C, 9·23% H, 5·32% S.

5,6β-Cyclopropane-5β-cholestane-3β,19-diol 3-Acetate 19-Methanesulphonate (*III*)

The alcohol[1] *I* (700 mg) in pyridine (10 ml) was treated at 0°C with methanesulphonyl chloride (1 ml) and allowed to stand at 5°C for 4 h. The reaction mixture was worked up as described in the foregoing experiment to yield 720 mg of an oily product resisting all attempts at crystallization. $[\alpha]_D^{20}$ —12° (*c* 1·23). For $C_{31}H_{52}O_5S$ (536·8) calculated: 69·36% C, 9·77% H, 5·97% S; found: 69·09% C, 9·53% H, 5·90% S.

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3β-ol (*IV*)

a) *From* 5,6β-*cyclopropano*-5(10)a-*homo*-19-*nor*-5β-*cholest*-1(10)-*en*-3β-*ol* 3-*acetate* (V): The acetate *V* (1·2 g) was treated with a solution of potassium hydroxide (600 mg) in ethanol (40 ml) and allowed to stand at 60°C for 2 h. The excess alkali was removed with acetic acid, the solvents were distilled off under reduced pressure, the residue was diluted with water, and the product taken into ether. The ethereal solution was washed with a sodium hydrogen carbonate solution, water, dried, and ether evaporated. The crude product was crystallized from methanol to yield 830 mg of the alcohol *IV*, m.p. 105—106°C, $[\alpha]_D^{20}$ +162° (*c* 1·06). For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·31% C, 11·59% H.

b) *From* 5,6β-*cyclopropano*-5(10)a-*homo*-19-*nor*-5β-*cholest*-1(10)-*en*-3-*one* (VI): The ketone *VI* (2 g) in 1,2-dimethoxyethane (80 ml) was treated with solid lithium tri-tert-butoxyaluminium hydride (4 g) and allowed to stand at room temperature for 1 h. The reaction mixture was diluted with ether, poured into 2% hydrochloric acid. The organic layer was worked up and ether distilled off. The residue was chromatographed over silica gel (150 g) in benzene. Fractions with the polar component were combined, solvent removed, and the residue was crystallized from methanol to yield 230 mg of the alcohol *IV*, m.p. 108—109°C, $[\alpha]_D^{20}$ +174° (*c* 1·32).

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3β-ol 3-Acetate (*V*)

a) *From* 5,6β-*cyclopropano*-5β-*cholestane*-3β,19-*diol* 3-*acetate* 19-p-*toluenesulphonate* (II) *with sodium iodide*: The tosylate *II* (1·5 g) in 1,2-dimethoxyethane (90 ml) was heated to 90°C under

stirring with sodium iodide (3 g) for 3 h. Fresh sodium iodide was added (3 g) and the reaction mixture was treated similarly for another 3 h. After cooling off ether was added, the solids were filtered off and the filtrate was washed with hydrochloric acid (2%), a sodium hydrogen carbonate solution, water, dried, and ether removed. The residue was chromatographed on a silica gel column (300 g) in benzene. The corresponding fractions were worked up and the residue was crystallized from methanol to yield 950 mg of the acetate *V*, m.p. 93—94°C, $[\alpha]_D^{20}$ +151° (*c* 1·37). Mass spectrum: $M^{+\bullet}$ 440. IR spectrum: 1738, 1244, 1022 (acetate), 1662, 3055 cm^{-1} (double bond). ^{1}H-NMR spectrum: 0·30—0·55 (m, two cyclopropane protons), 0·67 (s, 18-H), 0·85 (d, J = 6·5 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H), 1·98 (s, acetate), 2·23 and 2·65 (two m, J_1 = 6·5 Hz, J_2 = 10 Hz, $J_3 = J_{gem}$ = 12·5 Hz, 2-H), 4·57 (*m*, $W_{1/2}$ = 30 Hz, 3α-H), 5·29 (t, $J_1 = J_2$ = 6·5 Hz, 1-H). For $C_{30}H_{48}O_2$ (440·7) calculated: 81·76% C, 10·98% H; found: 81·81% C, 10·74% H.

b) *From* II *on acetolysis*: The tosylate *II* (2·5 g) was refluxed with anhydrous sodium acetate (2·5 g) in acetic acid (35 ml) and acetic anhydride (3·5 ml) for 5 h. The reaction mixture was diluted with water and the product taken into ether. The ethereal solution was washed with a sodium hydrogen carbonate solution, water, dried, and the product chromatographed over silica gel (150 g) in benzene. The lipophilic product which separated was crystallized from methanol to yield 1·1 g of the acetate *V*, m.p. 95—96°C, $[\alpha]_D^{20}$ +155° (*c* 1·08).

c) *From* II *by contact with silica gel*: The tosylate *II* (3 g) was dissolved in benzene and adsorbed on a silica gel column (400 g). After 20 h the steroid was eluted with benzene, the solvent was removed under reduced pressure and the residue was crystallized from methanol to yield 2·2 g of the acetate *V*, m.p. 95—96°C, $[\alpha]_D^{20}$ +153° (*c* 1·17).

d) *From* 5,6β-*cyclopropano*-5(10)a-*homo*-19-*nor*-5β-*cholest*-1(10)-*en*-3β-*ol* (IV): The alcohol *IV* (120 mg) in pyridine (2 ml) was acetylated with acetic anhydride (1·5 ml) for 18 h at room temperature. The reaction mixture was decomposed with ice and water, the product was extracted into ether, and the ethereal solution was worked up. The residue after evaporation of the solvent was crystallized from methanol to yield 85 mg of the acetate *V*, m.p. 97—98°C, $[\alpha]_D^{20}$ +158° (*c* 1·04).

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-10(1)-en-3-one (*VI*)

a) *From* 5,6β-*cyclopropano*-5(10)a-*homo*-19-*nor*-5β-*cholest*-1(10)-*en*-3β-*ol* (IV): The alcohol *IV* (1 g) in acetone (40 ml)was treated with excess Jones' reagent and allowed to stand for 10 min. The excess agent was removed with methanol, the mixture was diluted with water, and the product taken into ether. The ethereal solution was worked up and the residue after evaporation of the solvent was crystallized from methanol to yield 870 mg of the ketone *VI*, m.p. 104—105°C, $[\alpha]_D^{20}$ —31° (*c* 1·43). Mass spectrum: $M^{+\bullet}$ 396. IR spectrum: 1709 (carbonyl), 1658 cm^{-1} (double bond). CD spectrum: $\Delta\varepsilon_{224}$ +29·04, $\Delta\varepsilon_{257}$ 0, $\Delta\varepsilon_{300}$ —14·52. ^{1}H-NMR spectrum: 0·53 (m, two cyclopropane protons), 0·70 (s, 18-H), 0·85 (d, J = 6 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H), 3·66 (two d, J_1 = 6 Hz, J_2 = 12 Hz, 2-H), 5·25 (two d, J_1 = 6 Hz, J_2 = 8 Hz, 1-H). For $C_{28}H_{44}O$ (396·6) calculated: 84·78% C, 11·18% H; found: 84·76% C, 11·06% H.

b) *From* 5,6β-*cyclopropano*-5(10)a-*homo*-19-*nor*-5β-*cholest*-1(10)-*en*-3α-*ol* (VII): The alcohol *VII* (100 mg) was oxidized with Jones' reagent in acetone (3 ml) as described in the previous experiment. Similar working up and crystallization from methanol gave 67 mg of the ketone *VI*, m.p. 105°C, $[\alpha]_D^{20}$ —29° (*c* 0·98).

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3α-ol (*VII*)

The fractions with the lipophilic product from the chromatography of the 3β-epimer *IV* under *b*) were worked up and the residue was crystallized from methanol to yield 1·25 g of the alcohol *VII*, m.p. 86—87°C, $[\alpha]_D^{20}$ + 148° (*c* 1·33). For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·12% C, 11·48% H.

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3α-ol 3-Acetate (*VIII*)

The alcohol *VII* (200 mg) in pyridine (3 ml) was acetylated with acetic anhydride (2 ml) for 18 h at room temperature. Usual working up and crystallization from methanol afforded 175 mg of the acetate *VIII*, which resisted all attempts at crystallization; $[\alpha]_D^{20}$ + 164° (*c* 1·42). ^{1}H-NMR spectrum: 0·69 (s, 18-H), 0·86 (d, *J* = Hz, 26-H and 27-H), 0·89 (d, *J* = 6 Hz, 21-H), 1·97 (s, acetate), 5·03 (m, 3β-H), 5·20 (m, 1-H). For $C_{30}H_{48}O_2$ (440·7) calculated: 81·76% C, 10·98% H; found: 81·49% C, 10·83% H.

7β,19-Cyclo-B-homo-5α-cholestane-3β,5-diol (*IX*)

The diacetate *XI* (700 mg) in methanol (35 ml) was refluxed with a solution of potassium hydroxide (500 mg) in methanol (10 ml) for 3 h. Methanol was removed under reduced pressure, the residue was diluted with water, and the product extracted into ethyl acetate. The extract was washed with water, dried, and the product was crystallized from ethyl acetate to yield 520 mg of the diol *IX*, m.p. 180—182°C. $[\alpha]_D^{20}$ + 10° (*c* 1·17). Mass spectrum: $M^{+\cdot}$ 416. IR spectrum: 3 607, 1 072, 1 013 cm^{-1} (hydroxyl). For $C_{28}H_{48}O_2$ (416·7) calculated: 80·71% C, 11·61% H; found: 80·67% C, 11·50% H.

7β,19-Cyclo-B-homo-5α-cholestane-3β,5-diol 3-Monoacetate (*X*)

The diol *IX* (800 mg) in pyridine (4 ml) was acetylated with acetic anhydride (2·5 ml) for 20 h at room temperature. The reaction mixture was decomposed with ice and water, and the product was isolated with ether. Usual working up afforded a product which was chromatographed over silica gel (80 g) in benzene–ether (9 : 1). Fractions with the polar component were combined, solvents removed, and the residue was crystallized from methanol–water to yield 620 mg of the monoacetate *X*, m.p. 131—132°C, $[\alpha]_D^{20}$ 0° (*c* 1·33). Mass spectrum: $M^{+\cdot}$ 458. IR spectrum: 3 615 (hydroxyl), 1 736, 1 255, 1 242, 1 026 cm^{-1} (acetate). For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·57% C, 10·76% H.

7β,19-Cyclo-B-homo-5α-cholestane-3β,5-diol 3,5-Diacetate (*XI*)

a) *From* 5,6β-*cyclopropano*-5β-*cholestane*-3β,19-*diol* 3-*acetate* 19-p-*toluenesulphonate* (II): Elution of the chromatography after isolation of the acetate *V* under *b*) afforded fractions with the polar component. Working up and evaporation of the solvent yielded 1·1 g of a crude product which on crystallization from methanol gave 910 mg of the diacetate *XI*, m.p. 108—109°C, $[\alpha]_D^{20}$ 0° (*c* 1·17). Mass spectrum: $M^{+\cdot}$ 500. IR spectrum: 1 738, 1 730, 1 242, 1 025 cm^{-1} (acetate). ^{1}H-NMR spectrum: 0·67 (s, 18-H), 0·86 (d, *J* = 6 Hz, 21-H, 26-H, and 27-H), 1·98 (s, two acetates), 4·93 (m, *W* = 28 Hz, 3α-H). For $C_{32}H_{52}O_4$ (500·7) calculated: 76·75% C, 10·47% H; found: 76·70% C, 10·36% H.

b) *From* 7β,19-*cyclo*-B-*homo*-5α-*cholestane*-3β,5-*diol* (IX): The fractions with the lipophilic product from the chromatography of the monoacetate *X* were worked up and the residue was crystallized from methanol to yield 170 mg of the diacetate *XI*, m.p. 107—108°C, $[\alpha]_D^{20}$ 0° (*c* 1·08).

7β,19-Cyclo-B-homo-5α-cholestan-5-ol-3-one (*XII*)

a) *From* 7β,19-*cyclo*-B-*homo*-5α-*cholestane*-3β,5-*diol* (IX): The diol *IX* (450 mg) in acetone (50 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 10 min. The excess oxidizing agent was removed with methanol, part of the solvents were distilled off under reduced pressure, the residue was diluted with water, and the product was taken into ether. The ethereal solution was worked up and solvents removed. The crude product was crystallized from methanol to yield 330 mg of the ketone *XII*, m.p. 159—160°C, $[\alpha]_D^{20}$ +47° (*c* 1·18). Mass spectrum: $M^{+\cdot}$ 414. IR spectrum: 3610, 1081 (hydroxyl), 1707, 1693 cm^{-1} (carbonyl). For $C_{28}H_{46}O_2$ (414·6) calculated: 81·10% C, 11·18% H; found: 81·06% C, 11·00% H.

b) *From* 7β,19-*cyclo*-B-*homo*-5α-*cholestane*-3α5,-*diol* (XIII): The diol *XIII* (90 mg) was oxidized with Jones' reagent in acetone (5 ml) as described in the foregoing experiment. Similar working up and crystallization from methanol gave 54 mg of the ketone *XII*, m.p. 156—158°C, $[\alpha]_D^{20}$ +45° (*c* 0·89).

7β,19-Cyclo-B-homo-5α-cholestane-3α,5-diol (*XIII*)

The diacetate *XIV* (400 mg) in ethanol (20 ml) was refluxed with a solution of potassium hydroxide (300 mg) in ethanol (15 ml) for 2 h. The excess alkali was removed with acetic acid and the solvents were distilled off *in vacuo*. The residue was diluted with water and the product taken into ethyl acetate. The extract was washed with a sodium hydrogen carbonate solution, dried, and solvent removed. The product was crystallized from ethyl acetate to yield 245 mg of the diol *XIII*, m.p. 174—175°C, $[\alpha]_D^{20}$ +56° (*c* 1·29). IR spectrum: 3621 cm^{-1} (hydroxyl). ^{1}H-NMR spectrum: 0·67 (s, 18-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·92 (d, J = 6 Hz, 21-H), 4·01 (m, $W_{1/2}$ = 23 Hz, 3β-H). For $C_{28}H_{48}O_2$ (416·7) calculated: 81·10% C, 11·18% H; found: 79·96% C, 11·06% H.

7β,19-Cyclo-B-homo-5α-cholestane-3α,5-diol 3,5-Diacetate (*XIV*)

The ketol *XII* (1·2 g) in 1,2-dimethoxyethane (35 ml) was treated with solid lithium tri-tert-butoxyaluminium hydride (3 g) and allowed to stand at room temperature for 30 min. The mixture was poured on ice, acidified with 2% hydrochlorid acid and the product was extracted with ethyl acetate. The extract was worked up and solvent distilled off *in vacuo*. The crude diol was acetylated with acetic anhydride (5 ml) in pyridine (7 ml) at 70°C for 14 h. The reaction mixture was decomposed with ice and water, the product was isolated with ether and the solution was worked up. The crude product after evaporation of the solvent was crystallized from methanol until the traces of the slightly more lipophilic epimeric diacetate *XI* were removed. Yield 820 mg of the diacetate, *XIV*, m.p. 126—128°C, $[\alpha]_D^{20}$ +189° (*c* 1·76). Mass spectrum: $M^{+\cdot}$ 500. For $C_{32}H_{52}O_4$ (500·7) calculated: 76·75% C, 10·47% H; found: 76·68% C, 10·24% H.

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β,10α-cholestan-3β-ol (*XV*)

The unsaturated alcohol *IV* (2·2 g) in glacial acetic acid (50 ml) was hydrogenated over Adams' catalyst (200 mg) for 2 h. The catalyst was filtered off, washed with ether, and the filtrate was diluted with ether (200 ml). The solution was washed with water, a sodium hydrogen carbonate

solution, dried, and solvent removed. The residue was chromatographed on a silica gel column (200 g) in benzene–ether (19 : 1). Fractions with the polar product were worked up, solvent removed, and the residue was crystallized from methanol to yield 1·05 g of the alcohol *XV*, 111—112°C, $[\alpha]_D^{20}$ +58° (*c* 1·32). Mass spectrum: $M^{+\cdot}$ 400. IR spectrum: 3625, 1037, 1028 (hydroxyl), 3055 cm^{-1} (cyclopropane). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·85% C, 11·94% H.

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β,10α-cholestan-3β-ol 3-Acetate (*XVI*)

The alcohol *XV* (230 mg) in pyridine (3 ml) was acetylated with acetic anhydride (2 ml) for 18 h at room temperature. Usual working up and crystallization from methanol gave 195 mg of the acetate *XVI*, m.p. 111—112°C, $[\alpha]_D^{20}$ +52° (*c* 1·08). Mass spectrum: $M^{+\cdot}$ 442. ^{1}H-NMR spectrum: 0·22—0·47 (m, cyclopropane protons), 0·63 (s, 18-H), 0·86 (d, J = 6 Hz, 21-H, 26-H and 27-H), 1·98 (s, acetate), 4·73 (m, $W_{1/2}$ = 32 Hz, 3α-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·27% C, 11·22% H.

5-Methyl-5(10)a-homo-19-nor-5β,10α-cholestan-3β-ol (*XVII*)

Fractions with the lipophilic component from the chromatography of the alcohol *XV* were combined, solvent removed, and the residue was crystallized from methanol to yield 620 mg of the alcohol *XVII*, m.p. 108—109°C, $[\alpha]_D^{20}$ +3° (*c* 1·64). Mass spectrum: $M^{+\cdot}$ 402. For $C_{28}H_{50}O$ (402·7) calculated: 83·51% C, 12·52% H; found: 83·42% C, 12·47% H.

5-Methyl-5(10)a-homo-19-nor-5β,10α-cholestan-3β-ol 3-Acetate (*XVIII*)

The alcohol *XVII* (250 mg) was acetylated with acetic anhydride (2 ml) in pyridine (3 ml) for 20 h at room temperature. Usual working up and crystallization from methanol gave 180 mg of the acetate *XVIII*, m.p. 92—93°C, $[\alpha]_D^{20}$ −5° (*c* 1·17). Mass spectrum: $M^{+\cdot}$ 444. ^{1}H-NMR spectrum: 0·66 (s, 18-H), 0·85 (d, J = 6 Hz, 26-H and 27-H), 0·87 (d, J = 6 Hz, 21-H), 0·91 (s, 5-methyl), 2·02 (s, acetate), 5·08 (m, $W_{1/2}$ = 18 Hz, 3α-H). For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 80·89% C, 11·62% H.

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β,10α-cholestan-3-one (*XIX*)

a) *From* 5,6β-*cyclopropano*-5(10)a-*homo*-19-*nor*-5β,10α-*cholestan*-3β-*ol* (XV): The alcohol *XV* (500 mg) in acetone (20 ml) was treated with excess Jones' reagent and set aside for 15 min. Methanol was added, the mixture was diluted with water, and the product was taken into ether. The ethereal solution was worked up and ether removed. The residue was crystallized from methanol to yield 415 mg of the ketone *XIX*, m.p. 97—98°C, $[\alpha]_D^{20}$ +77° (*c* 1·28). Mass spectrum: $M^{+\cdot}$ 398. IR spectrum: 3060 (cyclopropane), 1705 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{294}$ +0·34. ^{1}H-NMR spectrum: 0·25—0·58 (m, cyclopropane protons), 0·62 (s, 18-H), 0·84 (d, J = 6 Hz, 26-H and 27-H), 0·85 (d, J = 6 Hz, 21-H). For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·27% C, 11·58% H.

b) *From* 5,6β-*cyclopropano*-5(10)a-*homo*-19-*nor*-5β,10α-*cholestan*-3α-*ol* (XX): The alcohol *XX* (115 mg) was oxidized with Jones' reagent in acetone (4 ml) as described in the foregoing experiment. Similar working up and crystallization from methanol yielded 80 mg of the ketone *XIX*, m.p. 97—98°C, $[\alpha]_D^{20}$ +76° (*c* 1·08).

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β,10α-cholestan-3α-ol (*XX*)

The alcohol *VII* (1·8 g) in acetic acid (30 ml) was hydrogenated over Adams' catalyst (200 mg) as described for the 3β-epimer *XV*. Similar working up afforded a crude product which was chromatographed over silica gel (150 g) in benzene. Fractions with the lipophilic product were combined, solvent removed, and the residue was crystallized from methanol to yield 650 mg of the alcohol *XX*, m.p. 132—133°C. $[\alpha]_D^{20}$ +9° (*c* 1·43). Mass spectrum: $M^{+\cdot}$ 400. For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·71% C, 11·82% H.

5,6β-Cyclopropano-5(10)a-homo-19-nor-5β,10α-cholestan-3α-ol 3-Acetate (*XXI*)

The alcohol *XX* (200 mg) was acetylated with acetic anhydride (2 ml) in pyridine (3 ml) at room temperature for 24 h. Usual working up and crystallization from methanol yielded 140 mg of the acetate *XXI*, m.p. 62°C, $[\alpha]_D^{20}$ +58° (*c* 1·34). ^{1}H-NMR spectrum: 0·17—0·43 (m, two cyclopropane protons), 0·65 (s, 18-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·87 (d, J = 6 Hz, 21-H), 2·02 (s, acetate), 5·13 (m, $W_{1/2}$ = 9 Hz, 3β-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·26% C, 11·17% H.

5-Methyl-5(10)a-homo-19-nor-5β,10α-cholestan-3α-ol (*XXII*)

Elution of the chromatography after isolation of the 3β-epimer *XX* afforded fractions with the polar compound. Working up and crystallization from methanol gave 720 mg of the alcohol *XXII*, m.p. 122—123°C, $[\alpha]_D^{20}$ +9° (*c* 1·63). Mass spectrum: $M^{+\cdot}$ 402. For $C_{28}H_{50}O$ (402·7) calculated: 83·51% C, 12·52% H; found: 83·38% C, 12·40% H.

5-Methyl-5(10)a-homo-19-nor-5β,10α-cholestan-3α-ol 3-Acetate (*XXIII*)

The alcohol *XXII* (130 mg) in pyridine (2 ml) was acetylated with acetic anhydride (1·5 ml) at room temperature for 18 h. Usual working up and crystallization from methanol yielded 105 mg of the acetate *XXIII*, m.p. 117°C, $[\alpha]_D^{20}$ +19° (*c* 1·07). ^{1}H-NMR spectrum: 0·65 (s, 18-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·89 (d, J = 6 Hz, 21-H), 0·97 (s, 5-methyl), 1·97 (s, acetate), 4·83 (m, $W_{1/2}$ = 25 Hz, 3β-H). For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 80·73% C, 11·72% H.

5-Methyl-5(10)a-homo-19-nor-5β,10α-cholestan-3-one (*XXIV*)

a) *From 5-methyl-5(10)a-homo-19-nor-5β,10α-cholestan-3β-ol* (XVII): The alcohol *XVII* (200 mg) in acetone (8 ml) was oxidized with excess Jones' reagent at room temperature for 10 min. Methanol was added, the mixture was diluted with water, and the product taken into ether. Working up and crystallization from methanol gave 165 mg of the ketone *XXIV*, m.p. 86—87°C, $[\alpha]_D^{20}$ —13° (*c* 1·53). Mass spectrum: $M^{+\cdot}$ 400. IR spectrum: 1 709, 1 694 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{290}$ —2·00. ^{1}H-NMR spectrum: 0·67 (s, 18-H), 0·85 (d, J = 6 Hz, 26-H and 27-H), 0·90 (s, 5-methyl). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·91% C, 11·95% H.

b) *From 5-methyl-5(10)a-homo-19-nor-5β,10α-cholestan-3α-ol* (XXII): Oxidation of the alcohol *XXII* (115 mg) in acetone (8 ml) as described above and similar working up gave 86 mg (methanol) of the ketone *XXIV*, m.p. 85—87°C. $[\alpha]_D^{20}$ —15° (*c* 1·08).

5,6β-Cyclopropano-5β-cholestan-3β-ol-19-oic Acid Methyl Ester 3-Acetate (*XXV*)

The alcohol *I* (2 g) in acetone (80 ml) was treated with excess Jones' reagent and heated to 50°C for 3 h. The excess reagent was removed with methanol, the mixture was diluted with water, and the product taken into ether. The ethereal solution was washed with water, dried, and ether removed. The residue was dissolved in methanol (8 ml) and ether (60 ml) and treated with excess diazomethane in ether. After 10 min at room temperature the excess diazomethane was removed with acetic acid, the reaction mixture was washed with a sodium hydrogen carbonate solution, water, dried, and the solvents were distilled off *in vacuo*. The crude product was purified by column chromatography (150 g of silica gel in benzene) to remove polar impurities and crystallized from methanol to yield 1·75 g of the methyl ester *XXV*, m.p. 102—103°C, $[\alpha]_D^{20}$ —12° (*c* 1·64). For $C_{31}H_{50}O_4$ (486·7) calculated: 76·50% C, 10·36% H; found: 76·39% C, 10·21% H.

[19-$^2H_2$]-5,6β-Cyclopropano-5β-cholestane-3β,19-diol (*XXVI*)

The ester *XV* (500 mg) was dissolved in absolute ether (40 ml) and treated with lithium aluminium deuteride (150 mg). After 30 min at room temperature the mixture was decomposed with ice and water, diluted with ether, and acidified with 2% hydrochloric acid. The ethereal layer was worked up, and the residue was crystallized from methanol–water to yield 380 mg of the diol *XXVI*, m.p. 150—151°C, $[\alpha]_D^{20}$ —10° (*c* 1·03), in accordance with the literature[1]. Mass spectrum: $M^{+\cdot}$ 418.

[19-$^2H_2$]-5,6β-Cyclopropano-5β-cholestane-3β,19-diol 3-Monoacetate (*XXVII*)

The diol *XXVI* (360 mg) in pyridine (5 ml) was treated with acetic anhydride (0·5 ml) and allowed to stand at 0°C for 6 h. The mixture was decomposed with ice, diluted with water, and the product isolated with ether. Working up gave a crude product which was chromatographed on a silica gel column (30 g) in benzene. Fractions with the monoacetate were combined, solvent distilled off, and the residue was crystallized from ethanol–water to yield 210 mg of the monoacetate *XXVII*, m.p. 97—98°C, $[\alpha]_D^{20}$ —3° (*c* 0·76), in accordance with the literature[1]. Mass spectrum: $M^{+\cdot}$ 460.

[19-$^2H_2$]-5,6β-Cyclopropano-5β-cholestane-3β,19-diol 3-Acetate 19-*p*-Toluene sulphonate (*XXVIII*)

The monoacetate *XXVII* (480 mg) was transformed into the tosylate *XXVIII* as described for the unlabelled derivative *II*. Crystallization of the crude product from methanol–ether yielded 450 mg of the tosylate *XXVIII*, m.p. 144—145°C, $[\alpha]_D^{20}$ —16° (*c* 1·06).

[5(10)a-$^2H_2$]-5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3β-ol (*XXIX*)

The acetate *XXX* (280 mg) was hydrolysed with ethanolic potassium hydroxide as described for the unlabelled compound *IV* under *a*) to yield 210 mg of the alcohol *XXIX*, m.p. 105—106°C, $[\alpha]_D^{20}$ +165° (*c* 1·03). Mass spectrum: $M^{+\cdot}$ 400.

[5(10)a-$^2H_2$]-5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3β-ol 3-Acetate (*XXX*)

The tosylate (*XXVIII*) 430 mg) was submitted to the sodium iodide reaction in 1,2-dimetoxy-ethane as described for the unlabelled compound *V* under *a*). Similar working up and crystalliza-

tion from methanol afforded 220 mg of the acetate *XXX*, m.p. 93—94°C, $[\alpha]_D^{20}$ +154° (*c* 0·75). Mass spectrum: $M^{+\cdot}$ 442.

[5(10)a-$^2H_2$]-5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3-one (*XXXI*)

The alcohol *XXIX* (180 mg) was oxidized with Jones' reagent in acetone as described for the unlabelled compound *VI*. Crystallization of the crude product from methanol yielded 145 mg of the ketone *XXXI*, m.p. 104—105°C, $[\alpha]_D^{20}$ —30° (*c* 1·02). Mass spectrum: $M^{+\cdot}$ 398.

[5(10)a-$^2H_2$]-5,6β-Cyclopropano-5(10)a-homo-19-nor-5β-cholest-1(10)-en-3α-ol (*XXXII*)

The ketone *XXXI* (140 mg) was reduced with lithium tri-tert-butoxyaluminium hydride as described for the 3β-epimer *IV* under *b*). The mixture of the alcohols *XXIX* and *XXXII* was separated by preparative TLC in benzene–ether (9 : 1). The zone with the lipophilic compound was worked up, the product extracted with chloroform, and solvent removed. The residue was crystallized from methanol to yield 95 mg of the labelled alcohol *XXXII*, m.p. 87°C, $[\alpha]_D^{20}$ +152° (*c* 0·79). Mass spectrum: $M^{+\cdot}$ 400.

Deuterium Exchange in 7β,19-Cyclo-B-homo-5α-cholestan-5-ol-3-one (*XII*)

The ketone *XII* (2 mg) in tetrahydrofuran (1 ml) was stirred with lithium deuteroxide (2 mg), decyltrimethylammonium bromide (1 mg) and deuterium oxide (2 ml) in an argon atmosphere at 20°C for 48 h. The aqueous layer was saturated with potassium carbonate, the organic products were taken into benzene (5 ml), and the solvents were evaporated *in vacuo*. The residue was dissolved in [O-^{2}H] ethanol (0·2 ml) and an aliquot was evaporated into the ion source.

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