ABSOLUTE CONFIGURATION AT $C_{(20)}$ OF THE DERIVATIVES OF 21-NOR-5α-CHOLANE-20,24-DIOL*

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Derivatives of 21-nor-5α-cholane-20,24-diol *XI* and *XIX* were prepared by stepwise construction of the side-chain in the position 17β.Their absolute configuration at $C_{(20)}$ was determined on the basis of chemical correlation with the derivatives of 21-nor-5α-cholan-20-ol, *XVI* and *XXIV*. The absolute configuration of alcohols *XVI* and *XXIV* was determined from the ratio of the yields in which they are formed during the reduction of ketone *X* and using the benzoate rule. To compounds *XI*—*XVIII* the configuration 20*R* and to compounds *XIX*—*XXVI* the configuration 20*S* has been assigned.

In connection with our studies of steroids with polysubstituted side-chain[1,2] we needed derivatives of 21-nor-5α-cholane-20,24-diol of known absolute configuration at $C_{(20)}$.

In order to simplify the interpretation of spectral measurements and to make chromatographic separation of compounds easier the initial study was carried out with derivatives of 5α-cholane substituted in the side chain only. As starting material ketone *I* was used which was degraded to hydroxy acid *II* by a known procedure[3]. The acid was esterified with dimethyl sulfate in the presence of potassium carbonate[4] to methyl ester *III*. Its hydroxy group in the position 3β was eliminated by reduction of the corresponding mesylate *IV* with zinc and sodium iodide in 1,2-dimethoxyethane[5,6] under formation of methyl ester *V*. On condensation of ester *V* with the sodium salt of dimethyl sulfoxide[7–9] a mixture of two diastereoisomeric keto sulfoxides *VI* was obtained, differing by configuration on the sulfur atom. The ratio of both diastereoisomers was determined on the basis of their ^{1}H-NMR spectra, by comparison with corresponding 3β-acetoxy 5,6-unsaturated derivatives[4]. From the ratio of the intensities of the methyl group (SO—CH_3) signals and the AB system of the methylene protons (CO—CH_2—SO) the ratio of the *R* to *S* diastereoisomers can be determined; it is in the 1·5 – 1·7 range.

Alkylation of the sodium salt of keto sulfoxide *VI* with ethyl bromoacetate[4] and subsequent reduction of the alkylation product *VII* with amalgamated aluminum[8,10]

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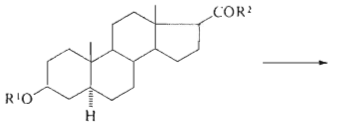
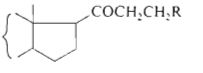
afforded γ-keto ester *IX*. Its reduction with lithium aluminum hydride afforded two 1,4-diols *XI* and *XIX*. The less polar diol prevailed over the more polar diol *XIX* in a 5 : 2 ratio. The absolute configuration at $C_{(20)}$ in both diols was determined on the basis of chemical correlation with derivatives of 5α-cholan-20-ol (*XVI* and

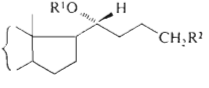


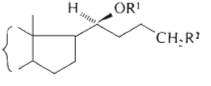
I, R^1 = Ac, R^2 = CH_3
II, R^1 = H, R^2 = OH
III, R^1 = H, R^2 = OCH_3
IV, R^1 = Mes, R^2 = OCH_3

V, R = OCH_3
VI, R = CH_2SOCH_3
VII, R = $CH(SOCH_3)CH_2COOCH_2CH_3$
VIII, R = $CH(SOCH_3)CH_2CH_3$



IX, R = $COOCH_2CH_3$
X, R = CH_3





XI, R^1 = H, R^2 = OH
XII, R^1 = H, R^2 = $OOCC(CH_3)_3$
XIII, R^1 = CH_3, R^2 = $OOCC(CH_3)_3$
XIV, R^1 = CH_3, R^2 = OH
XV, R^1 = CH_3, R^2 = OMes
XVI, R^1 = R^2 = H
XVII, R^1 = CH_3, R^2 = H
XVIII, R^1 = Bz, R^2 = H

XIX, R^1 = H, R^2 = OH
XX, R^1 = H, R^2 = $OOCC(CH_3)_3$
XXI, R^1 = CH_3, R^2 = $OOCC(CH_3)_3$
XXII, R^1 = CH_3, R^2 = OH
XXIII, R^1 = CH_3, R^2 = OMes
XXIV, R^1 = R^2 = H
XXV, R^1 = CH_3, R^2 = H
XXVI, R^1 = Bz, R^2 = H

XXIV). Acylation of diol *XI* with pivalic acid chloride monopivalate *XII* was obtained which was methylated to O-methyl derivative *XIII* with diazomethane and aluminum chloride. Its ester group was split off using lithium aluminum hydride under formation of hydroxy derivative *XIV*. After elimination of the hydroxyl group in the position 24 by reduction of the corresponding mesylate *XV* with zinc and sodium iodide in 1,2-dimethoxyethane[5,6] methyl ether *XVII* was obtained. Diol *XIX* was converted to methyl ether *XXV* analogously, *via* the intermediates *XX* – *XXIII*.

For an unambiguous synthesis of methyl ethers *XVII* and *XXV* the following procedure was employed. On alkylation of the sodium salt of keto sulfoxide *VI* with ethyl iodide[11] and subsequent reduction of the alkylation product *VIII* with amalgamated aluminum in aqueous tetrahydrofuran[8,10] ketone *X* was obtained. Its structure is confirmed by the carbonyl group band ($\nu_{(C=O)} = 1707\ cm^{-1}$) in the infrared spectrum and the following ions in its mass spectrum: M^+ of the composition $C_{23}H_{38}O$, $M^+ - C_3H_7$ of the composition $C_{20}H_{31}O$ and $M^+ - C_3H_7CO$ of the composition $C_{19}H_{31}$. On reduction of ketone *X* with sodium borohydride two alcohols, *XVI* and *XXIV*, were formed in a 5 : 1, and on reduction with sodium in 1-propanol the same alcohols were formed in a 1 : 4 ratio. On the basis of the known course[12] of the reduction of steroidal 20-oxo derivatives configuration 20*R* may be assigned to alcohol *XVI* and the absolute 20*S* configuration to alcohol *XXIV*. In order to confirm the configurations proposed corresponding benzoates *XVIII* and *XXVI* were prepared from alcohols *XVI* and *XXIV* respectively. The value $\Delta M_D = M_{D(benzoate)} - M_{D(alcohol)}$ corresponds[13] in the case of compounds *XVI* and *XVIII* ($\Delta M_D = -26°$) to configuration 20*R* and in the case of compounds *XXIV* and *XXVI* ($\Delta M_D = +26°$) to configuration 20*S*. Further, corresponding methyl ethers *XVII* and *XXV* were prepared from alcohols *XVI* and *XXIV*. Methyl ether *XVII*, prepared from alcohol *XVI* is identical with the methyl ether prepared from diol *XI*, and methyl ether *XXV* prepared from alcohol *XXIV* is identical with the methyl ether prepared from diol *XIX*. From this the absolute configuration 20*R* follows for diol *XI* and the absolute configuration 20*S* for diol *XIX*.

EXPERIMENTAL

The melting points were determined on a Kofler block. Optical rotations were measured in chloroform with a ±3° accuracy. The infrared spectra were recorded on a Zeiss UR-20 instrument in tetrachloromethane, unless stated otherwise. The ^{1}H-NMR spectra were measured on a Tesla B 476 (60 MHz) instrument in deuteriochloroform at 30°C using tetramethylsilane as internal reference. The chemical shifts are given in ppm of the δ-scale. The apparent coupling constants were obtained from the first order analysis. The mass spectra were measured on a JEOL JMS D-100 apparatus using direct inlet technique. For column chromatography silica gel according to Pitra (60—120 μ) and neutral alumina (Reanal, activity II), were used, while for thin-layer chromatography (TLC) silica gel G (Merck) was employed. The "working up the ethereal extracts in a conventional manner" means, that they were washed with dilute hydrochloric acid (1 : 4), water, saturated aqueous solution of potassium hydrogen carbonate, water, dried over

anhydrous sodium sulfate and the solvent evaporated in a vacuum. Samples for analysis were dried at 50°C and 26 Pa for 12 h. The identity of the samples prepared in various ways was checked by comparison of their infrared spectra, thin-layer chromatography and mixture melting point determination.

17β-Methoxycarbonyl-5α-androstan-3β-ol (*III*)

A solution of sodium hypobromite (prepared from 14·5 g of sodium hydroxide, 124 ml of water, 14·85 g of bromine and 83 ml of dioxane according to ref.[3]) was added into a solution of 10 g of ketone *I* in a mixture of 346 ml of dioxane and 111 ml of water under cooling at +5°C. The mixture was stirred at room temperature for 3 h and then a solution of 3·5 g of sodium sulfite in 35 ml of water was added to it and the mixture refluxed for 15 min. After acidification with hydrochloric acid (17·5 ml) of the still hot solution and dilution with 160 ml of water the reaction mixture was allowed to stand overnight in a refrigerator. The separated product was filtered off under suction, washed with water and dried over phosphorus pentoxide in a vacuum. Yield, 8·5 g of acid *II*, m.p. 247—249°C (acetone–ether), literature[14] gives m.p. 249—250°C. Potassium carbonate (9·62 g) and dimethyl sulfate (5·85 g) were added to a solution of 7·42 g of acid *II* in 70 ml of acetone and the mixture was refluxed for 3 h under stirring. It was diluted with 150 ml of ether and filtered through a column of alumina (30 g). The column was washed with dichloromethane. Crystallization of the residue from ether gave 6 g of methyl ester *III*, m.p. 174—175°C, $[\alpha]_D$ +53° (*c* 1·9). Literature[15] gives m.p. 170°C, $[\alpha]_D$ +52°. IR spectrum (chloroform): 1 725, 1 200, 1 160 ($COOCH_3$), 3 610, 1 038 (OH) cm^{-1}.

17β-Methoxycarbonyl-5α-androstane (*V*)

Methanesulfonyl chloride (2 ml) was added to a cooled solution (at —5°C) of hydroxy derivative *III* (4 g) in pyridine (30 ml) and the mixture was allowed to stand at 0°C for 1 h. After pouring on ice the separated product was filtered off under suction, washed with water and dissolved in a mixture of dichloromethane and ether (1 : 3). The organic phase was worked up in the conventional manner. The residue (5 g) was dissolved in a mixture of 50 ml of 1,2-dimethoxyethane and 5 ml of water, zinc powder (7·5 g) was added followed by sodium iodide (8·5 g), and the mixture refluxed for 8 h. After dilution with ether (200 ml) and filtration through a layer of diatomaceous earth it was washed with dilute hydrochloric acid (1 : 4), water, saturated potassium hydrogen carbonate solution, 5% aqueous sodium thiosulfate solution and water. Crystallization of the residue from methanol afforded 3 g of methyl ester *V*, m.p. 141—143°C, $[\alpha]_D$ +45° (*c* 1·8). Literature[16] gives m.p. 142°C, $[\alpha]_D$ +48°.

21-Methylsulfinyl-5α-pregnan-20-one (*VI*)

A solution of methyl ester *V* (2 g) in tetrahydrofuran (55 ml) was added to a solution of sodium hydride (1·5 g) in dimethyl sulfoxide (45 ml), prepared according to lit.[7—9], over 10 min. After 2 h stirring under nitrogen at room temperature the mixture was poured into water, neutralized with solid ammonium chloride and extracted with ethyl acetate. The organic phase was washed 6 times with water. The residue (2·5 g) contained according to TLC predominantly keto sulfoxide *VI*. ^{1}H-NMR spectrum: 0·65 bs (3 H, 18-H), 0·79 s (3 H, 19-H), 2·69 s (1·8 H, SCH_3 *S*-(*R*) isomer), 2·71 s (1·2 H, SCH_3 *S*-(*S*) isomer), 3·73 and 3·84 AB system J_{gem} = —14·4 Hz (1·27 H, $COCH_2SO$ *S*-(*R*) isomer), 3·67 and 3·97 AB system J_{gem} = —14·4 Hz (0·73 H, $COCH_2SO$ *S*-(*S*) isomer).

Ethyl Ester of 20-Oxo-21-nor-5α-cholan-24-oic Acid (*IX*)

Keto sulfoxide *VI* (1·95 g) was added to a suspension of sodium hydride (290 mg) in tetrahydrofuran (20 ml). When the development of hydrogen ceased a solution of ethyl bromoacetate (1 ml) in tetrahydrofuran (3 ml) was added to the mixture under stirring and cooling with ice and salt, and stirred for another 2 h at room temperature. The reaction was carried out under nitrogen. The mixture was poured into an aqueous solution of ammonium chloride and extracted with ethyl acetate. The extract was washed with water. The residue (2·1 g) contained according to TLC predominantly compound *VII*. Amalgamated aluminum (4 g) was then added to a solution of 1·1 g of the crude product *VII* in a mixture of tetrahydrofuran (100 ml) and water (10 ml). After 2 h refluxing and stirring the mixture was filtered through a layer of diatomaceous earth, the inorganic salt was washed with a mixture of benzene and ether (1 : 1), and the combined organic phases were washed with water. The residue was chromatographed on a column of silica gel (100 g) with a mixture of light petroleum and ethyl acetate (98 : 2). The eluate contained 410 mg of ketoester *IX*, m.p. 134—135°C (ether), $[\alpha]_D$ +83·6° (*c* 1·5). IR spectrum (chloroform): 1 705 (C=O), 1 726 ($COOC_2H_5$) cm^{-1}. ^{1}H-NMR spectrum: 0·59 s (3 H, 19-H), 0·78 s (3 H, 18-H), 2·62 mt (4 H, $COCH_2CH_2COO$), 1·23 t (3 H) and 4·12 q (2 H) J = 7 Hz (CH_3CH_2OOC). For $C_{24}H_{40}O_3$ (388·6) calculated: 77·27% C, 10·38% H; found: 77·00% C, 10·34% H.

21-Nor-5α-cholan-20-one (*X*)

Keto sulfoxide *VI* (728 mg) was added to a suspension of sodium hydride (50 mg) in dimethyl sulfoxide (25 ml) and stirred for 2 min. Ethyl iodide (312 mg) was then added and the mixture stirred under nitrogen and at room temperature for 2·5 h. After pouring into water and neutralization with solid ammonium chloride the product was extracted with ethyl acetate and the extract washed with water (6 times). The residue was dissolved in a mixture of tetrahydrofuran (80 ml) and water (8 ml) and amalgamated aluminum (2·5 g) was added to it. After 2 h refluxing and stirring the mixture was filtered through diatomaceous earth and the inorganic salts were washed with ether. The combined organic phases were washed with 5% aqueous sodium thiosulfate and water. The residue (800 mg) was chromatographed on a silica gel column (80 g) with light petroleum–ether (99 : 1). Ketone *X* (500 mg) was eluted which was crystallized from ether–methanol mixture to afford 340 mg of pure ketone *X*, m.p. 85—88°C, $[\alpha]_D$ +97° (*c* 1·0). IR spectrum: 1 707, 1 408 ($CO—CH_2$) cm^{-1}. ^{1}H-NMR spectrum: 0·58 s (3 H, 19-H), 0·76 s (3 H, 18-H), 2·36 mt ($CH_2—CO$). Mass spectrum *m/e*: 330 ($C_{23}H_{38}O$, M^+); 315 ($M^+—CH_3$), 312 ($M^+—H_2O$), 297 ($M^+—CH_2—H_2O$), 287 ($C_{20}H_{31}O$, $M^+—C_3H_7$), 259 ($C_{19}H_{31}$, $M^+—C_3H_7CO$). For $C_{23}H_{38}O$ (330·6) calculated: 83·57% C, 11·59% H; found: 83·55% C, 11·70 % H.

(20*R*)-21-Nor-5α-cholane-20,24-diol (*XI*)

Lithium aluminum hydride (100 mg) was added to a solution of γ-keto ester *IX* (80 mg) in ether (30 ml) and refluxed for 2 h. The reaction mixture was decomposed with water, the product extracted with ether and the extract worked up in the conventional manner. The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in benzene–acetone (4 : 1) (double development). The zone containing the less polar component was eluted with acetone. Yield, 31 mg of diol *XI*, m.p. 168—170°C (ether), $[\alpha]_D$ +20·6° (*c* 1·9). IR spectrum (chloroform): 3 638, 3 472 (OH) cm^{-1}. For $C_{23}H_{40}O_2$ (348·6) calculated: 79·25% C, 11·57% H; found: 79·54% C, 11·27% H.

(20*R*)-21-Nor-5α-cholane-20,24-diol 24-Monopivalate (*XII*)

Pivaloyl chloride (0·6 ml) was added to a solution of 110 mg of diol *XI* in 5 ml of pyridine and the mixture allowed to stand at room temperature for 2 h. After pouring onto ice the product was extracted with ether and the extract worked up in the conventional manner. The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (4 : 1). Yield, 160 mg of monopivalate *XII*, m.p. 105—107°C (ether), $[\alpha]_D$ +13° (*c* 1·7). IR spectrum: 1728, 1397, 1366, 1158 (OOC–$C(CH_3)_3$), 3636, 3608 shoulder (OH) cm^{-1}. For $C_{28}H_{48}O_3$ (432·7) calculated: 77·73% C, 11·18% H; found: 78·00% C, 11·09% H.

(20*R*)-20-Methoxy-21-nor-5α-cholan-24-ol 24-Pivalate (*XIII*)

Ethereal diazomethane solution (10 ml) was added to a solution of 57 mg of monopivalate *XII* in 2 ml of dichlormethane and the mixture was cooled with ice. Anhydrous aluminum chloride (40 mg) was then added in three portions over 1 h. The mixture was diluted with ether (100 ml), filtered through diatomaceous earth and the ethereal solution was worked up in the conventional manner. The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (9 : 1). The yield of methyl ether *XIII* was 47 mg, m.p. 99—101°C (acetone), $[\alpha]_D$ −3·3° (*c* 2·1). IR spectrum: 1728, 1397, 1366, 1159 ($OOC(CH_3)_3$), 2825 shoulder (OCH_3) cm^{-1}. ^{1}H-NMR spectrum: 0·66 s (3 H, 19-H); 0·77 s (3 H, 18-H); 1·18 s (9 H, $OOCC(CH_3)_3$); 3·24 mt, $W \approx 21$ Hz (20-H); 4·07 bt, $J \approx 6$ Hz (24-H_2). For $C_{29}H_{50}O_3$ (446·7) calculated: 77·97% C, 11·28% H; found: 78·06% C, 11·61% H.

(20*R*)-20-Methoxy-21-nor-5α-cholan-24-ol (*XIV*)

Lithium aluminium hydride (100 mg) was added into a solution of 130 mg of ester *XIII* in 20 m of ether. After 1 h refluxing under stirring the mixture was decomposed with water, the product extracted with ether and the extract worked up in the conventional manner. Chromatography of the residue on preparative silica gel plate (20 × 20 cm) in light petroleum–acetone (4 : 1) gave 90 mg of oily alcohol *XIV*, $[\alpha]_D$ +5° (*c* 1·3). IR spectrum: 3638, 3437 (OH) cm^{-1}. For $C_{24}H_{42}O_2$ (362·6) calculated: 79·50% C, 11·68% H; found: 79·36% C, 11·96% H.

(20*R*)-21-Nor-5α-cholan-20-ol (*XVI*)

a) Sodium borohydride (240 mg) was added into a solution of ketone *X* (200 mg) in a mixture of benzene (20 ml) and methanol (20 ml) under cooling with ice and stirring. After 2 h stirring at room temperature the mixture was poured into water, acidified with hydrochloric acid, and the product was extracted with ether and the extract worked up in the usual manner. The residue was chromatographed on 3 preparative silica gel plates (20 × 20 cm) in benzene–ether (97 : 3). The zones containing the less polar substance were combined and eluted with dichloromethane. Yield, 150 mg of alcohol *XVI*, m.p. 146—147°C (ether), $[\alpha]_D$ +18° (*c* 1·2). IR spectrum: 3631, 3610 shoulder (OH) cm^{-1}. For $C_{23}H_{40}O$ (332·6) calculated: 83·07% C, 12·12% H; found: 83·05% C, 12·26% H.

b) Sodium (1 g) was added into a solution of 150 mg of ketone *X* in a mixture of benzene (10 ml) and 1-propanol (15 ml) under sttiring and refluxing over 1 h. After cooling the mixture was diluted with ether (100 ml) and poured into water, the organic phase was worked up in the usual manner. The residue was chromatographed on 2 preparative silica gel plates (20 × 20 cm) in light petroleum–ether (7 : 3). Elution of the combined zones containing the less polar substance gave 20 mg of alcohol *XVI*, m.p. 144—146°C (ether).

(20*R*)-20-Methoxy-21-nor-5α-cholane (*XVII*)

a) Methyl iodide (0·7 ml) was added into a suspension of 50 mg of sodium hydride in a solution of 50 mg of alcohol *XVI* in tetrahydrofuran (3 ml). After 3 h stirring at 40°C under nitrogen the mixture was poured into water, the product extracted with ether and the extract worked up in the conventional manner. Chromatography of the residue on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (97 : 3) afforded 35 mg of methyl ether *XVII*, m.p. 67 to 69°C (ether), $[\alpha]_D$ —1° (*c* 2·1). IR spectrum: 1100 (C—O—C) cm^{-1}. ^{1}H-NMR spectrum: 0·66 s (3 H, 19-H), 0·84 s, (3 H, 18-H), 3·16 mt, $W \approx 30$ Hz (20-H), 3·28 s (OCH_3). For $C_{24}H_{42}O$ (346·6) calculated: 83·17% C, 12·21% H; found: 83·47% C, 12·17% H.

b) Methanesulfonyl chloride (0·5) ml was added into a solution of 50 mg of hydroxy derivative *XIV* in 2 ml of pyridine at —10°C. After 2 h standing at the same temperature the mixture was poured onto ice, the product extracted with ether and the extract worked up in the usual manner. The residue (according to TLC pure mesylate *XV*) was dissolved in a mixture of 4 ml of 1,2-dimethoxyethane and 0·4 ml of water, 300 mg of sodium iodide and 260 mg of zinc powder were added, and the reaction mixture refluxed for 3 h. After filtering through a small column of alumina (10 g) it was eluted with ether. The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (97 : 3). Yield, 20 mg of methyl ether *XVII*, m.p. 66—68°C (methanol), $[\alpha]_D$ —3° (*c* 1·1).

(20*R*)-21-Nor-5α-cholan-20-ol 20-Benzoate (*XVIII*)

Benzoyl chloride (0·1 ml) was added to a solution of 50 mg of alcohol *XVI* in 2 ml of pyridine and the mixture heated at 40°C for 4 h. Then the mixture was poured onto ice and the product extracted with ether. The extract was worked up in the conventional manner and the residue chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (97 : 3). Yield, 60 mg of oily benzoate *XVIII*, $[\alpha]_D$ +8·3° (*c* 0·9). IR spectrum: 1714, 1603, 1492, 1487, 1212, 711 (C_6H_5COO) cm^{-1}. ^{1}H-NMR spectrum: 0·67 s (3 H, 19-H); 0·71 s (3 H, 18-H); 5·25 mt, $W \approx 20$ Hz (20-H); 7·50 mt and 8·07 mt (C_6H_5COO). For $C_{30}H_{44}O_2$ (436·7) calculated: 82·52% C, 10·16% H; found: 82·81% C, 10·12% H.

(20*S*)-21-Nor-5α-cholane-20,24-diol (*XIX*)

The zone with the more polar substance (preparation of diol *XI*) was eluted with acetone. Yield, 8 mg of diol *XIX*, m.p. 181—183°C (tetrachloromethane), $[\alpha]_D$ −4° (*c* 1·2; chloroform–methanol 10 : 3). IR spectrum (chloroform): 3628, 3420, 3325, 3260 (OH) cm^{-1}. For $C_{23}H_{40}O_2$ (348·6) calculated: 89·25% C, 11·57% H; found: 79·47% C, 11·41% H.

(20*S*)-21-Nor-5α-cholan-20-ol (*XXIV*)

a) Elution of the zones containing the more polar substance (preparation of compound *XVI*, procedure *a*)) gave 28 mg of alcohol *XXIV*, m.p. 99—100°C (acetone).

b) The combined zones containing the more polar substance (preparation of compound *XVI*, procedure *b*)) were eluted with ether. Yield, 80 mg of alcohol *XXIV* m.p. 103—105°C (acetone), $[\alpha]_D$ +7·2° (*c* 1·3). IR spectrum (chloroform): 3528 (OH) cm^{-1}. For $C_{23}H_{40}O$ (332·6) calculated: 83·07% C, 12·12% H; found: 82·86% C, 12·39% H.

(20*S*)-20-Methoxy-21-nor-5α-cholane (*XXV*)

a) Methyl iodide (1 ml) was added to a suspension of 100 mg of sodium hydride in a solution of 50 mg of alcohol *XXIV* in 3 ml of tetrahydrofuran and the mixture was stirred at 40°C and under nitrogen for 4 h. After decomposition with water the product was extracted with ether and the extract worked up in the conventional manner. Chromatography of the residue on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (97 : 3) gave 45 mg of methyl ether *XXV*, m.p. 65—66°C (methanol), $[\alpha]_D$ +18° (*c* 1·3). IR spectrum: 1093 (C—O—C) cm^{-1}. ^{1}H-NMR spectrum: 0·66 s (3 H, 19-H); 0·78 s (3 H, 18-H); 3·03 mt (20-H); 3·25 s (OCH_3). For $C_{24}H_{42}O$ (346·6) calculated: 83·17% C, 12·21% H; found: 82·90% C, 12·18% H.

b) Pivaloyl chloride (0·15 ml) was added into a solution of 30 mg of diol *XIX* in 2 ml of pyridine and the mixture was left to stand for 2 h. After pouring onto ice the product was extracted with ether and the extract worked up in the usual manner. The residue (45 mg) was dissolved in 2 ml of dichloromethane and additioned with 10 ml of ethereal diazomethane solution. The mixture was cooled with ice, then anhydrous aluminum chloride (40 mg) was added in three portions over 1 h. The reaction mixture was diluted with ether (100 ml), filtered through diatomaceous earth and the ethereal solution was worked up in the conventional manner. The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (9 : 1). Yield, 35 mg of amorphous methyl ether *XXI*. IR spectrum: 1727, 1398, 1365, 1158 ((OOCC.$(CH_3)_3$), 2826 shoulder (OCH_3) cm^{-1}. Lithium aluminum hydride (30 mg) was added into a solution of 35 mg of ester *XXI* in 5 ml of ether. After 1 h refluxing under stirring the mixture was decomposed with water, the product extracted with ether and the extract worked up in the usual manner. Methanesulfonyl chloride (0·25 ml) was added at —10°C to the residue (25 mg) dissolved in 1 ml of pyridine. After 2 h standing at —10°C the mixture was poured onto ice, the product was extracted with ether and the extract worked up in the conventional manner. The residue was dissolved in a mixture of 2 ml of 1,2-dimethoxyethane and 0·2 ml of water, sodium iodide (150 mg) and zinc dust (130 mg) were added to it and the mixture was refluxed for 3 h under stirring. After filtration through a column of alumina (5 g), the column was washed with ether. The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (97 : 3). Yield, 11 mg of methyl ether *XXV*, m.p. 64—66°C (methanol), $[\alpha]_D$ +17° (*c* 2·0).

(20*S*)-21-Nor-5α-cholan-20-ol 20-Benzoate (*XXVI*)

Benzoyl chloride (0·1 ml) was added into a solution of 50 mg of alcohol *XXIV* in 2 ml of pyridine and the mixture allowed to stand at room temperature for 17 h. The mixture was poured onto ice and the product extracted with ether. The extract was worked up in the conventional manner. Chromatography of the residue on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (95 : 5) gave 57 mg of benzoate *XXVI*, m.p. 106—108°C (ether), $[\alpha]_D$ +12° (*c* 2·1). IR spectrum: 1718, 1276 (C_6H_5COO) cm^{-1}. ^{1}H-NMR spectrum: 0·68 s (3 H, 19-H); 0·76 s (3 H, 18-H); 5·29 mt, W = 21 Hz (20-H); 7·49 mt and 8·06 mt (C_6H_5COO). For $C_{30}H_{44}O_2$ (436·7) calculated: 82·52% C, 10·16% H; found: 82·45% C, 9·87% H.

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