PREPARATION AND ABSOLUTE CONFIGURATION AT $C_{(20)}$ OF 21-NOR-5α-CHOLAN-24→20-OLIDE DERIVATIVES*

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The lactones *X* and *XI* were obtained on reaction of the aldehyde *III* with lithium salt of methyl propinoate followed by hydrogenation of the intermediary esters *IV* and *V*. Treatment of the epoxides *XXI* and *XXII* with dilithium salt of acetic acid yielded the lactones *X* and *XI*. These lactones were also obtained by reaction of the epoxides *XXI* and *XXII* with sodium diethyl malonate through intermediates *XXIII* and *XXV*. The preparation of α-methylene lactones *XXVII* and *XXVIII* is also described. The 20*R* configuration was established for the lactones *X*, *XXIII* and *XXVII* while the lactones *XI*, *XXV* and *XXVIII* were assigned the 20*S* configuration both on the basis of ^{1}H-NMR spectra and chemical correlations.

In the preceding communication[1] we reported the preparation of 20,24-disubstituted derivatives of 21-nor-5α-cholane with a flexible side chain. In the present paper we describe the preparation of 21-nor-5α-cholane derivatives with a side chain containing a γ-lactone five-membered ring with the oxygen bridge linking the 20 and 24 positions.

The first approach utilized the known[1] keto ester *XII*. The literature reports[2] reduction of its 3β-acetoxy-5,6-unsaturated analog with sodium borohydride to yield an unseparable mixture of γ-lactones in which the authors assume the 20*R* isomer to be the preponderant component. Reduction of the keto ester *XII* with sodium borohydride gave a chromatographically homogeneous product in which the IR-spectroscopy demonstrated the presence of a γ-lactone ring. However, reduction of this product with sodium bis(2-methoxyethoxy)aluminum hydride gave rise to the diols *VII* and *IX* in 9 : 1 relation. This result shows that the γ-lactone obtained by the above reduction is in fact a mixture of the lactones *X* and *XI* in 9 : 1 relation. Comparing the optical rotation value of the afore-mentioned mixture with the values for pure lactones *X* and *XI* (their preparation is described below) permits to estimate the proportion of the lactone *X* to 89% whereas comparison of the CD values leads to 91% content of this lactone.

Since we did not succeed in separation of the two lactones by means of available chromatographic methods, it appeared necessary to work out procedures for preparation of each individual isomer in pure condition.

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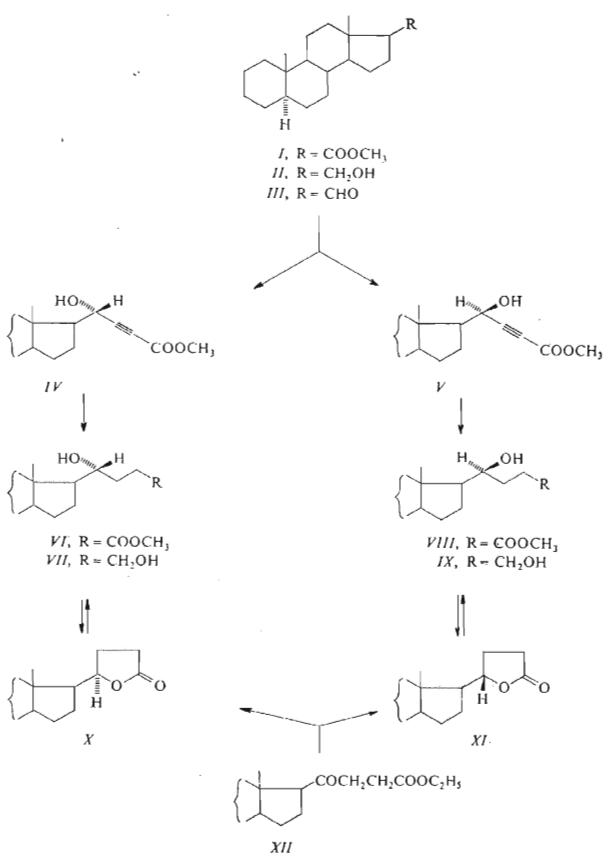
The first route sets out from the aldehyde *III* obtained by oxidation of the alcohol *II* with pyridinium chlorochromate: the alcohol *II* was prepared from the methyl ester *I* using the known procedure[3]. Reaction of the aldehyde *III* with lithium salt of methyl propinoate[4] afforded two hydroxy esters *IV* and *V* which were separated by chromatography on a silica gel column. Their absolute configuration at $C_{(20)}$ was assigned



I, R = $COOCH_3$
II, R = CH_2OH
III, R = CHO

IV *V*

VI, R = $COOCH_3$
VII, R = CH_2OH

VIII, R = $COOCH_3$
IX, R = CH_2OH

X *XI*

XII

on the basis of differences in chemical shifts of 18-H_3 signals in the ^{1}H-NMR spectra (Table I). According to the literature[5] in 20-hydroxy steroids containing a 22,23-triple bond and possessing a (20*S*)-configuration the 18-H_3 signal is shifted downfield as compared with the respective (20*R*)-derivatives. It is thus possible to assign the(20*S*)--configuration for the compound *IV*, and the configuration 20*R* for the compound *V*.

Hydrogenation of the unsaturated hydroxy ester *IV* gives rise to the saturated hydroxy ester *VI* which cyclizes extremely readily to the γ-lactone *X*. Reduction of the latter compound with sodium bis(2-methoxyethoxy)aluminum hydride yields the known[1] diol *VII* with the (20*R*)-configuration. Analogously, the unsaturated hydroxy ester *V* gives rise to the saturated hydroxy ester *VIII* which is then converted into the γ-lactone *XI* and the latter reduced to the known[1] diol *IX* with the (20*S*)-configuration.

The aldehyde *III*, requisite as starting material for the above described synthesis of the lactones *X* and *XI*, was prepared from the methyl ester *I*. This ester was obtained[1] on degradation of the pregnane side chain with the loss of one of its carbon atoms while the subsequent synthesis of the lactone ring required lengthening of the side chain by three carbon atoms. We therefore attempted to work out a synthesis starting directly from the pregnane derivative. One of the possibilities appeared to be opening of the oxirane ring of the epoxides *XXI* and *XXII* by dilithium salt of acetic acid[6].

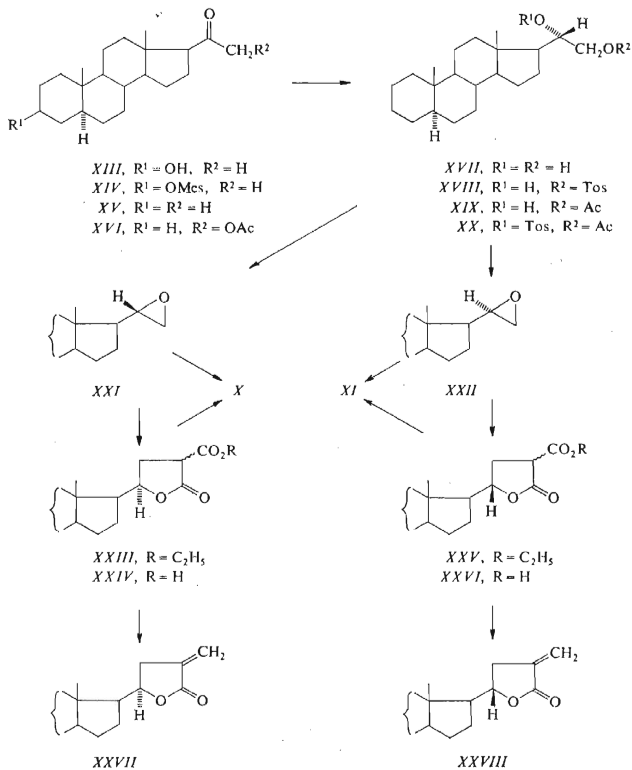
The epoxides *XXI* and *XXII* were prepared in the following manner. The hydroxy group in the hydroxy ketone *XIII* was removed by the application of the known[7,8] procedure *via* the mesylate *XIV* to give the ketone *XV*. Acetoxylation[9] of the ketone *XV* at position 21 gave the acetoxy ketone *XVI* which was converted into the diol *XVII* by lithium aluminum hydride reduction (TLC analysis revealed the presence of only a trace amount of the epimeric diol of the (20*R*)-configuration). Partial tosylation of the diol *XVII* led to the monotosylate *XVIII* which on treatment with potassium carbonate in methanol gave the 20*S*-epoxide *XXI*.

The (20*R*)-epoxide *XXII* was prepared by using a modification of the known method[10]. Reduction of the acetoxy ketone *XVI* with sodium borohydride at 0°C yielded practically pure monoacetate *XIX* which was tosylated to the tosyl acetate *XX* and the latter purified by crystallization. On treatment with sodium methoxide in methanol the tosyl acetate *XX* yielded the (20*R*)-epoxide *XXII*.

Reaction of the (20*S*)-epoxide *XXI*, with the dilithium salt of acetic acid afforded the (20*R*)-lactone *X*. Analogously, the epoxide *XXII* with the (20*R*)-configuration gives the (20*S*)-lactone *XI*. These results are in conformity with configurations assigned on the basis of ^{1}H-NMR spectra of the esters *IV* and *V* and on the basis of chemical correlations with the diols *VII* and *IX*.

In the alternate procedure, the oxirane ring of the epoxide *XXI* was opened with sodium diethyl malonate[11] and the intermediary α-ethoxycarbonyl-γ-lactone *XXIII* was decarboxylated[12] by treatment with water and sodium chloride in dimethyl

sulfoxide at 170°C to yield the lactone *X*. The lactone *XI* was prepared in the same manner from the epoxide *XXII*. The both methods give comparable yields of the lactones *X* and *XI*; with dilithium salt of acetic acid the yield is 75% and 70%, respectively, while the yield achieved with sodium diethyl malonate was 70% and 60%, respectively. Using the known procedure[11,13], the α-ethoxycarbonyl-γ-lactones *XXIII* and *XXV* were converted into α-methylene lactones *XXVII* and *XXVIII* through intermediary α-carboxy-γ-lactones *XXIV* and *XXVI*.



EXPERIMENTAL

Melting points were determined on a Kofler block. Optical rotations were measured in chloroform with an error of $\pm 3°$. The IR spectra were recorded on a Zeiss UR—20 spectrometer in tetrachloromethane unless stated otherwise. The CD spectra were recorded on a Roussel-Jouan Dichrographe II in dioxane. Silica gel prepared according to Pitra and neutral aluminum oxide (Reanal, activity II) were used for column chromatography whereas silica gel G (Merck) was used for thin layer chromatography. Silica gel G impregnated with sodium tetraborate[14] was used for checking the purity of the compound *XVII* by thin layer chromatography. Usual work up of an ethereal solution means washing the solution with dilute hydrochloric acid (1 : 4), water, saturated aqueous potassium hydrogen carbonate solution, water, drying with anhydrous sodium sulfate and evaporation of the solvent *in vacuo*. Analytical samples were dried at 50°C and 26 Pa for 12 h. The identity of samples prepared by different routes was checked by comparison of their IR spectra, by thin layer chromatography (TLC) and mixture melting point determination.

17β-Formyl-5α-androstane (*III*)

Pyridinium chlorochromate (5 g) was added to a solution of the alcohol *II* (5 g, m.p. 147—148°C; prepared following the literature[3]) in dichloromethane (100 ml). The mixture was stirred for 3 h at room temperature, then diluted with ether (100 ml) and passed through a column of alumina

TABLE I
Characteristic Parameters of ^{1}H-NMR Spectra

Compound[a]	18-H_3	19-H_3	20-H	21-H_2	23-H_2
III[b]	0·70 s	0·75 s	9·75 d $J = 2$	—	—
IV[b,c]	0·73 s	0·77 s	4·38 bd $J \approx 9$	—	—
V[b,d]	0·69 s	0·77 s	4·30 mt $W \approx 14$	—	—
X[b]	0·74 s	0·78 s	4·38 mt $W \approx 22$	—	2·37 mt
XI[b]	0·70 s	0·78 s	4·38 mt $W \approx 22$	—	2·37 mt
XX[b,e]	0·70 s	0·74 s	4·83 mt $W \approx 18$	4·06 mt	—
XXI[f]	0·79 s	0·79 s	2·85 mt	2·38 mt 2·67 mt	—
XXII[f]	0·75 s	0·79 s	2·85 mt	2·41 mt 2·68 mt	—
XXVII[f,g]	0·76 s	0·78 s	4·43 mt $W \approx 23$	—	—
XXVIII[f,h]	0·72 s	0·78 s	4·42 mt $W \approx 23$	—	—

[a] The spectra were measured in deuteriochloroform with tetramethylsilane as internal reference. Chemical shifts are given in ppm (δ-scale); coupling constants (J) and widths of multiplets (W) are given in Hz. All values are obtained by first order analysis. [b] Measured on Tesla B 476 (60 MHz) instrument. [c] Other signal 3·75 s ($COOCH_3$). [d] Other signal 3·77 s ($COOCH_3$). [e] Other signals: 1·92 s ($OCOCH_3$); 2·40 s, 7·35 mt, 7·80 mt (*p*-toluenesulfonyl). [f] Measured on a Varian HA—100 (100 MHz) instrument. [g] Other signals 5·56 mt ($W = 9$) and 6·18 mt ($W = 8$) (23-methylene). [h] Other signals 5·55 mt ($W = 8$) and 6·16 mt ($W = 9$) (23-methylene).

(50 g). The column was eluted with ether, the solution evaporated to leave a residue (5 g) which was shown by TLC to be practically pure aldehyde *III*. IR spectrum: 2815 shoulder, 2713, 1721 (CHO) cm^{-1}.

Methyl (20*S*)-20-Hydroxy-21-nor-5α-chol-22-yn-24-oate (*IV*)

To a solution of diisopropylamine (1·4 ml) in tetrahydrofuran (10 ml) there was added in the course of 10 min 1·6M a solution of n-butyllithium in n-hexane (6·25 ml), after 30 min, methyl propinoate (0·95 ml) in the course of 10 min, after 80 min, a solution of the aldehyde *III* (1·1 g) in tetrahydrofuran (10 ml) in the course of 10 min. The reaction was conducted under argon at —78°C with stirring. After 5 h the mixture was decomposed with solid ammonium chloride and water, allowed to warm to the room temperature and diluted with saturated aqueous ammonium sulfate solution. The product was taken up in ether, the extract washed with saturated aqueous solution of potassium hydrogen carbonate and ammonium sulfate solution. The residue was chromatographed on a silica gel (100 g) column. The mixture of light petroleum–benzene–ether (95 : 95 : 10) eluted the ester *IV* (750 mg) m.p. 106—108°C and 113—115°C (light-petroleum), $[\alpha]_D$ —20° (*c* 1·8). IR spectrum: 3612 (OH), 2238 (C≡C), 1721, 1251 ($COOCH_3$) cm^{-1}. For $C_{24}H_{36}O_3$ (372·6) calculated: 77·38% C, 9·74% H; found: 77·74% C, 9·86% H.

Methyl (20*R*)-20-Hydroxy-21-nor-5α-chol-22-yn-24-ol (*V*)

Prolonged elution with the same mixture of solvents (preparation of the methyl ester *IV*) afforded the methyl ester *V* (410 mg), m.p. 153—155°C (light petroleum), $[\alpha]_D$ +6° (*c* 1·5). IR spectrum: 3614 (OH), 2238 (C≡C), 1721, 1252 ($COOCH_3$), cm^{-1}. For $C_{24}H_{36}O_3$ (372·6) calculated: 77·38% C, 9·74% H; found: 77·37% C, 9·95% H.

(20*R*)-21-Nor-5α-cholan-20,24-diol (*VII*)

A 70% benzene solution (0·3 ml) of sodium bis(2-methoxy ethoxy)aluminum hydride was added to a solution of the lactone *X* (30 mg) in benzene (5 ml) and refluxed while stirring for 2 h.The mixture was diluted with ether (30 ml) and worked up. The product was crystallized from ether to yield the diol *VII* (20 mg, m.p. 167—169°C) which proved identical with the authentic specimen[1].

(20*S*)-21-Nor-5α-cholan-20,24-diol (*IX*)

Reduction of the lactone *XI* (30 mg) was conducted in the same manner as that of the lactone *X*. Crystallization from tetrachloromethane yielded the diol *IX* (22 mg, m.p. 182—184°C) identical with the authentic sample[1].

(20*R*)-21-Nor-5α-cholan-24→20-olide (*X*)

a) A solution of the unsaturated ester *IV* (70 mg) in ethyl acetate (7 ml) was shaken with 10% palladium on charcoal (20 mg) under hydrogen at room temperature for 1 h, the catalyst filtered off and the filtrate evaporated under reduced pressure to yield pure (TLC) hydroxy ester *VI* (70 mg). IR spectrum: 1740 ($COOCH_3$), 3505 (OH) cm^{-1}. A solution of the hydroxy ester *VI* (60 mg) in tetrahydrofuran (7 ml) was treated with one drop of 70% perchloric acid for 15 min at room temperature. The mixture was diluted with ether (50 ml) and washed with potassium hydrogen carbonate solution and water. Evaporation of the solvent and crystallization of the residue from light petroleum gave the lactone *X* (40 mg), m.p. 204—206°C, $[\alpha]_D$ —13° (*c* 1·6).

IR spectrum: 1781, 1179 (γ-lactone) cm^{-1}. CD spectrum: $\Delta\varepsilon$ +0·77 (215 nm). For $C_{23}H_{36}O_2$ (344·5) calculated: 80·18% C, 10·53% H; found: 80·05% C, 10·68% H.

b) 1·6M Solution of n-butyllithium in n-hexane (4·1 ml) was added dropwise at —78°C to a stirred solution of diisopropylamine (668 mg) in tetrahydrofuran (11 ml) in the course of 10 min and the reaction mixture allowed to reach 0°C which required 30 min. The stirred solution was treated with a solution of acetic acid (0·189 ml) in tetrahydrofuran (2 ml) over a period of 5 min. The mixture was kept at 32°C for 30 min and then treated with a solution of the epoxide *XXI* (100 mg) in benzene (2 ml). The reaction was conducted under argon, the mixture was refluxed and stirred for 8 h, then decomposed with 2M-H_2SO_4 (30 ml), poured into water, the product taken up in ether, the solution washed with water and the solvent evaporated. The residue was chromatographed on two silica gel plates (20 × 20 cm) using a mixture of benzene–ether (93 : 7) for development. The product was crystallized from light petroleum to yield the lactone *X* (85 mg), m.p. 200—203°C, $[\alpha]_D$ —12° (*c* 2·2).

c) Sodium chloride (58 mg) and water (9 mg) were added to a solution of the crude lactone *XXIII* (100 mg) in dimethyl sulfoxide (10 ml). The mixture was stirred under nitrogen at 170°C for 6 h, after cooling diluted with ether (100 ml) and washed with water five times. Evaporation of the solvent and chromatography of the residue on a preparative silica gel plate (20 × 20 cm) using benzene–ether (93 : 7) for development furnished the lactone *X* (30 mg), m.p. 203—205°C (light petroleum), $[\alpha]_D$ —15° (*c* 1·1).

(20*S*)-21-Nor-5α-cholan-24→20-olide (*XI*)

a) The preparation of the lactone *XI* from the unsaturated ester *V* was performed through the hydroxy ester *VIII* (yield 72 mg of a product found to be homogeneous by TLC; IR spectrum: 1740 ($COOCH_3$), 3505, 3608 (OH) (cm^{-1}) in the same manner as preparation of the lactone *X* from the unsaturated ester *IV*. Crystallization from light petroleum gave the lactone *XI* (42 mg), m.p. 193—195°C, $[\alpha]_D$ +23° (*c* 1·2). IR spectrum: 1781, 1182, 1176 (γ-lactone) cm^{-1}. CD spectrum: $\Delta\varepsilon$ —1·07 (215 nm). For $C_{23}H_{36}O_2$ (344·5) calculated: 80·18% C, 10·53% H; found: 80·08% C, 10·33% H.

b) Preparation of the lactone *XI* from the epoxide *XXII* (100 mg) was performed in the same way as the lactone *X* from the epoxide *XXI*. Chromatography of the crude product on two silica gel plates (20 × 20 cm) yielded the lactone *XI* (40 mg), m.p. 193—195°C (light petroleum–ether), $[\alpha]_D$ +24° (*c* 1·1).

c) Preparation of the lactone *XI* from the crude lactone *XXV* (100 mg) was conducted in the same manner as that of the lactone *X* from the lactone *XXIII*. Chromatography of the crude product on a preparative silica gel plate (20 × 20 cm) in the system benzene–ether (93 : 7) afforded the lactone *XI* (24 mg) m.p. 194—196°C (light petroleum–ether), $[\alpha]_D$ +27° (*c* 1·5).

Reduction of the γ-Keto Ester *XII*

Sodium borohydride (200 mg) was added to a solution of the keto ester *XII* (ref.[1], 190 mg) in benzene (15 ml) and methanol (5 ml). The mixture was stirred at room temperature for 2 h, poured in water, acidified with hydrochloric acid and extracted with ether, the extract worked up in the usual manner and the residue after evaporation of the solvent was dissolved in benzene and the solution passed through a column of silica gel (5 g) using dichloromethane as eluant. This procedure yielded the mixture of the lactones *X* and *XI* (102 mg), m.p. 200—202°C (methanol) nol), $[\alpha]_D$ —9° (*c* 1·0). IR spectrum: 1781, 1180 (γ-lactone) cm^{-1}.

Reduction of the Mixture of the Lactones *X* and *XI*

The solution of the mixture of the lactones *X* and *XI* (270 mg) in benzene (22 ml) was treated under nitrogen with a 70% benzene solution of sodium bis(2-methoxyethoxy)aluminum hydride (1·3 ml) at reflux temperature for 2 h. The mixture was then diluted with ether (200 ml) and worked up. The residue was chromatographed on four silica gel plates (20 × 20 cm) that were developed twice in the system benzene–acetone (4 : 1). The less polar zones were collected and eluted with dichloromethane to yield the diol *VII* (240 mg), m.p. 167—169°C (ether), $[\alpha]_D$ +21° (*c* 1·9), identical with the autentic sample[1]. Elution of the more polar zones with acetone yielded the diol *IX* (26 mg), m.p. 183—186°C (tetrachloromethane), $[\alpha]_D$ —4° (*c* 1·2; chloroform–methanol 10 : 3), identical with the authentic sample[1].

21-Acetoxy-5α-pregnan-20-one (*XVI*)

Methanesulfonyl chloride (2 ml) was added to a solution of the alcohol *XIII* (4 g) in pyridine (30 ml) at —5°C. After 1 h standing at 0°C the mixture was poured on ice, the separed product was filtered by suction, washed with water and dissolved in a mixture of dichloromethane and ether (1 : 5). The organic phase was worked up, the residue after evaporation of the solvent was practically pure (TLC) mesylate *XIV* which was dissolved in a mixture of 1,2-dimethoxyethane (50 ml) and water (5 ml). Zinc powder (7·5 g) and sodium iodide (8·7 g) were added to this solution and the mixture was stirred and refluxed for 7·5 h, cooled, diluted with ether (300 ml) and filtered through a layer of kieselgur. The organic phase was washed with dilute hydrochloric acid, water, sodium hydrogen carbonate solution, saturated sodium thiosulfate solution and water. Evaporation of the solvent and crystallization from a mixture methanol–acetone–water yielded the ketone *XV* (2·5 g), m.p. 132—134°C, (literature[15] reports m.p. 136°C). To a solution of the ketone *XV* (2·5 g) in benzene (40 ml) were added at a time (over a period of 4 h); methanol (9·3 ml in 40 ml of benzene), boron trifluoride etherate (22·3 ml in 30 ml of benzene) and lead tetraacetate (5·93 g). The mixture was then diluted with ether (150 ml) and worked up as usual. Crystallization of the crude product from acetone–methanol–water gave the acetoxy ketone *XVI* (2 g), m.p. 199—201°C, $[\alpha]_D$ +94° (*c* 1·9). Literature[16] reports m.p. 201—202°C, $[\alpha]_D$ +98°.

(20*S*)-5α-Pregnane-20,21-diol 21-*p*-Toluenesulfonate (*XVIII*)

Lithium aluminum hydride (300 mg) was added to a solution of the acetoxy derivative *XVI* (900 mg) in tetrahydrofuran (30 ml) and benzene (10 ml), the mixture was stirred at room temperature for two h, decomposed with ethyl acetate and poured into diluted hydrochloric acid (1 : 4). The product was extracted with ethyl acetate and the extract worked up in the usual manner. Evaporation yielded a residue (850 mg) consisting (TLC analysis) of practically pure diol *XVII*. This diol (822 mg) was dissolved in pyridine (12 ml) and treated with *p*-toluenesulfonyl chloride (600 mg) at room temperature for 7 h. The mixture was poured onto ice, the product extracted with ether and the extract washed with dilute hydrochloric acid (1 : 4) and water, dried and evaporated. The residue was chromatographed on a column of silica gel (100 g). The mixture of light petroleum–benzene–ether (45 : 45 : 10) eluted non-polar impurities (70 mg) and a mixture of light petroleum–benzene–ether (40 : 40 : 20) eluted the monotosylate *XVIII* (860 mg), m.p. 133—135°C (light petroleum), $[\alpha]_D$ +8° (*c* 1·9). IR spectrum (chloroform): 1 365, 1 179 (*p*-toluenesulfonyl), 3 600 (OH) cm^{-1}. For $C_{28}H_{42}O_4S$ (474·7) calculated: 70·85% C, 8·92% H, 6·75% S; found: 70·70% C, 9·21% H, 6·51% S.

(20*S*)-5α-Pregnane-20,21-diol 20-*p*-Toluenesulfonate 21-Acetate (*XX*)

Sodium borohydride (306 mg) was added to a stirred solution of the ketone *XVI* (1·93 g) in a mixture of benzene (96 ml) and methanol (96 ml) at 0°C. Stirring was continued for 30 min under cooling. The mixture was acidified by acetic acid and evaporated to a small colume at reduced pressure, the residue was treated with dichloromethane and water, the organic layer was dried with sodium sulfate and the solvent evaporated. The residue was dissolved in pyridine (16 ml) and treated with *p*-toluenesulfonyl chloride (2·5 g) for 4 days. The mixture was then poured onto ice, separated product was filtered, washed with water, dissolved in benzene and worked up in usual manner. The residue was crystallized from ether to yield the tosylate *XX* (2·02 g), m.p. 182—183°C, $[\alpha]_D$ +12° (*c* 1·4). IR spectrum: 1748, 1232 (CH_3COO), 1378, 1189, 1179 (*p*-toluenesulfonyl) cm^{-1}. For $C_{30}H_{44}O_5S$ (516·7) calculated: 69·73% C, 8·58% H, 6·20% S; found: 69·46% C, 8·55% H, 6·15% S.

(20*S*)-20,21-Epoxy-5α-pregnane (*XXI*)

The tosylate *XVIII* (820 mg) in methanol solution (60 ml) was treated with anhydrous potassium carbonate (200 mg) at reflux temperature for 10 min with stirring. The solvent was then removed at reduced pressure, the residue dissolved in benzene and passed through a column of silica gel (25 g). Washing with benzene yielded the epoxide *XXI* (500 mg), m.p. 130—131°C (ether), $[\alpha]_D$ −19° (*c* 1·5). IR spectrum: 3045, 936, 870 (oxirane) cm^{-1}. For $C_{21}H_{34}O$ (302·5) calculated: 83·38% C, 11·33% H; found: 83·65% C, 11·23% H.

(20*R*)-20,21-Epoxy-5α-pregnane (*XXII*)

To a solution of sodium methoxide in methanol (prepared from 900 mg of sodium and 140 ml of methanol) was added a solution of the tosylate *XX* (2 g) in benzene (80 ml). The mixture was heated at 65°C under argon with stirring. After 30 min the solvent was removed at reduced pressure, the residue dissolved in benzene and passed through a column of silica gel (80 g). Washing with benzene yielded the epoxide *XXII* (1·13 g), m.p. 92—94°C (methanol–ether), $[\alpha]_D$ +5° (*c* 1·5). IR spectrum: 3042, 891 (oxirane) cm^{-1}. For $C_{21}H_{34}O$ (302·5) calculated: 83·38% C, 11·33% H; found: 83·47% C, 11·66% H.

(20*R*)-23ξ-Ethoxycarbonyl-21-nor-5α-cholan-24→20-olide (*XXIII*)

Diethyl malonate (1·2 ml) and a solution of the epoxide *XXI* (150 mg) in benzene (2 ml) were added to a solution of sodium (150 mg) in ethanol (4·6 ml). After stirring and heating to the reflux temperature under argon for 8 h, the mixture was diluted with ether (50 ml) and worked up. Evaporation gave a residue (400 mg) containing practically pure lactone *XXIII* and unreacted diethyl malonate (shown by TLC). An analytical sample was obtained by repeated crystallization from light petroleum. IR spectrum: 1787 (γ-lactone), 1741 ($COOC_2H_5$) cm^{-1}. For $C_{26}H_{40}O_4$ (416·6) calculated: 74·96% C, 9·68% H; found: 74·94% C, 9·82% H.

(20*S*)-23ξ-Ethoxycarbonyl-21-nor-5α-cholan-24→20-olide (*XXV*)

Preparation of the lactone *XXV* from the epoxide *XXII* (150 mg) was carried out in the same manner as preparation of the lactone *XXIII* from the epoxide *XXI* and gave a residue (423 mg) containing (TLC) practically pure lactone *XXV* and unreacted diethyl malonate. Analytical sample was obtained by repeated crystallization from light petroleum. IR spectrum: 1785 (γ-lac-

tone), 1742 ($COOC_2H_5$) cm^{-1}. For $C_{26}H_{40}O_4$ (416·6) calculated: 74·96% C, 9·68% H; found: 74·69% C, 9·32% H.

(20*R*)-23-Methylene-21-nor-5α-cholan-24→20-olide (*XXVII*)

Potassium hydroxide (1 g) in ethanol (10 ml) was added to a solution of crude lactone *XXIII* (300 mg) in ethanol (20 ml) and the mixture was refluxed for 1 h, poured onto ice and acidified with 4M-H_2SO_4. The product was taken up in ether, the extract washed with and evaporated to give a residue containing practically pure compound *XXIV* (TLC analysis). The latter was treated with 37% aqueous formaldehyde (6 ml) and diethylamine (1·2 ml) and after refluxing and stirring for 30 min the mixture was poured into diluted hydrochloric acid (1 : 4), the product extracted with ether and worked up. Chromatography of the residue on silica gel plate (20 × × 20 cm) using benzene–ether (96 : 4) for development yielded the lactone *XXVII* (50 mg), m.p. 179—181°C (light petroleum ether), $[\alpha]_D$ —21° (*c* 1·2). IR spectrum: 1771 (γ-lactone), 1669 (C=C) cm^{-1}. CD spectrum: $\Delta\varepsilon$ +0·79 (259 nm). For $C_{24}H_{36}O_2$ (356·6) calculated: 80·85% C, 10·18% H; found: 80·83% C, 10·29% H.

(20*S*)-23-Methylene-21-nor-5α-cholan-24→20-olide (*XXVIII*)

Preparation of the lactone *XXVIII* from the crude lactone *XXV* (300 mg) was carried out in the same manner as preparation of the lactone *XXVII* from the lactone *XXIII*. Chromatography of the crude reaction product on a silica gel plate (20 × 20 cm) in a benzene–ether (96 : 4) system yielded the lactone *XXVIII* (44 mg), m.p. 174—176°C (light petroleum–ether), $[\alpha]_D$ +34° (*c* 0·9). IR spectrum: 1771 (γ-lactone), 1669 (C=C) cm^{-1}. CD spectrum: $\Delta\varepsilon$ —1·19 (259 nm). For $C_{24}H_{36}O_2$ (356·6) calculated: 80·85% C, 10·18% H; found: 81·13% C, 9·88% H.

The analyses were carried out in the Analytical Laboratory of this Institute (head Dr J. Horáček). The infrared spectra were recorded by Mrs K. Matoušková and Mr P. Formánek and interpreted by Dr S. Vašíčková. CD spectra were recorded and interpreted by Dr S. Vašíčková. The ^{1}H-NMR *spectra were recorded by Dr M. Masojídková and Mrs J. Jelínková.*

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