PREPARATION AND ABSOLUTE CONFIGURATION AT $C_{(22)}$ OF 21,26,27-TRINOR-5α-CHOLESTAN-25→22-OLIDE DERIVATIVES*

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Epimeric 21,26,27-trinor-5α-cholestan-25→22-olides (*X* and *XVII*), 21,26,27-trinor-5α-cholest-23-en-25→22-olides (*XV* and *XXII*), and their 23-methyl derivatives *XVI* and *XXIII* were prepared by lengthening the side chain in 5α-pregnan-21-al (*I*). On the basis of CD spectra and chemical correlations with 21,26,27-trinor-5α-cholestane-22,25-diols, the configuration 22*S* was ascribed to lactones *X*, *XXII* and *XXIII* whereas lactones *XV*, *XVI* and *XVII* were assigned the 22*R* configuration.

In our previous paper[1] we published the preparation of 21,26,27-trinor-5α-cholestane-22,25-diol derivatives and determination of absolute configuration at $C_{(22)}$ in these compounds. In the present communication we describe synthesis of the corresponding lactones, *i.e.* derivatives of 21,26,27-trinor-5α-cholestan-25→22-olide.

The side chain of the aldehyde *I* was lengthened either by reaction with ethynylmagnesium bromide followed by elongation by one carbon atom[2], or by direct reaction with lithium salt of methyl propiolate[3]. In the former reaction route the aldehyde *I* (ref.[1]) afforded a 1 : 1 mixture of two acetylenic alcohols *II* and *VI* which were separated by preparative thin-layer chromatography. The hydroxy group in the alcohol *II* was protected as the tetrahydropyranyl ether. The protected compound *III*, after conversion into its lithium salt by reaction with butyllithium in hexane, was treated with methyl chloroformate to give the acetylenic ester *IV*. Removal of the protecting group with *p*-toluenesulfonic acid monohydrate in benzene–methanol mixture afforded the hydroxy ester *V* in 64% overall yield. The same reaction sequence was used for the preparation of the hydroxy ester *IX* (yield 64%) from the alcohol *VI via* the intermediates *VII* and *VIII*. The structure of the compound *V* was confirmed by its IR spectrum (3 612 and 3 415 cm^{-1}, (OH), 2 238 cm^{-1} (C≡C), 1 721 and 1 250 cm^{-1} (methyl ester)) and ^1H NMR spectrum (a $C_{(20)}$—H signal as a multiplet at $\delta = 4{\cdot}44$ and a methyl ester signal as a singlet at $\delta = 3{\cdot}76$). The main spectral parameters for the isomer *IX* were practically the same. The structure

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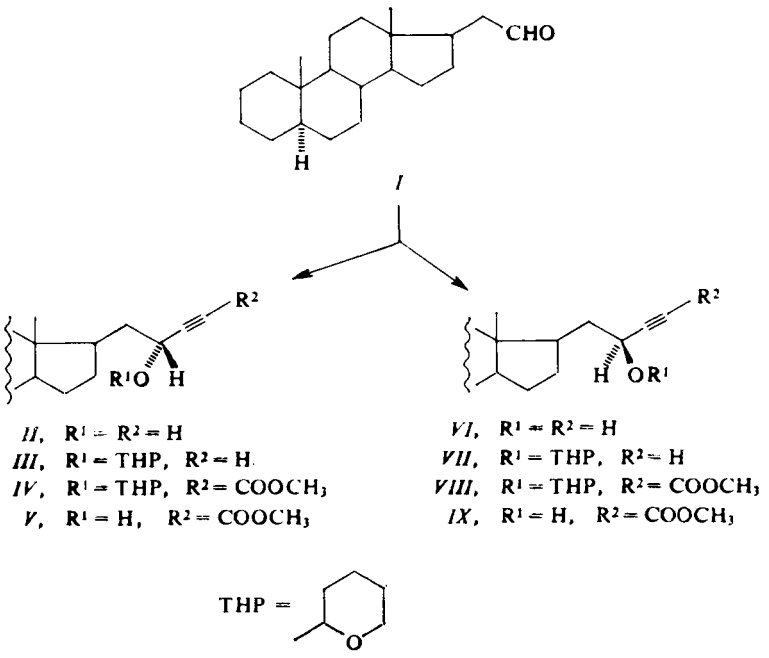
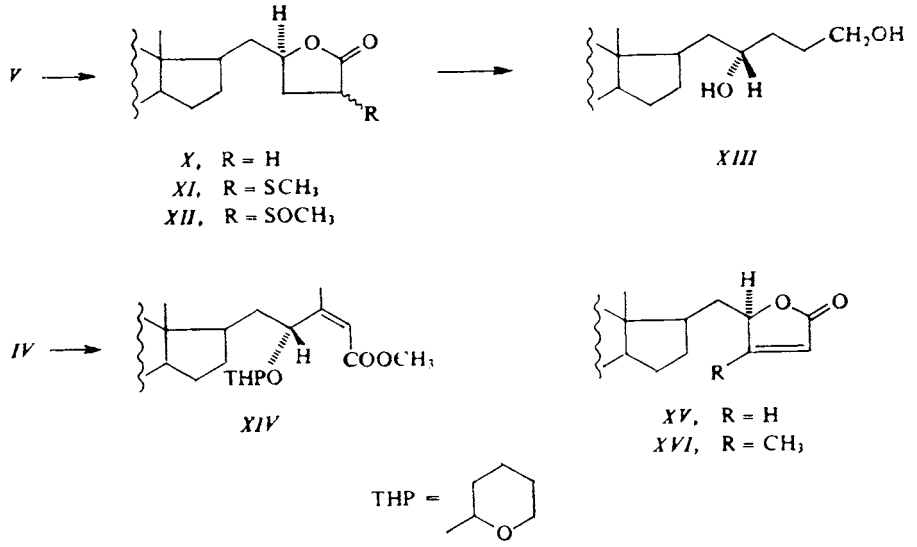
of the compounds *V* and *IX* was verified by their independent synthesis from the aldehyde *I*. Its reaction with lithium salt of methyl propiolate gave a mixture of both hydroxy esters *V* and *IX* from which equal amounts (23%) of each of the individual compounds were obtained by preparative thin-layer chromatography.



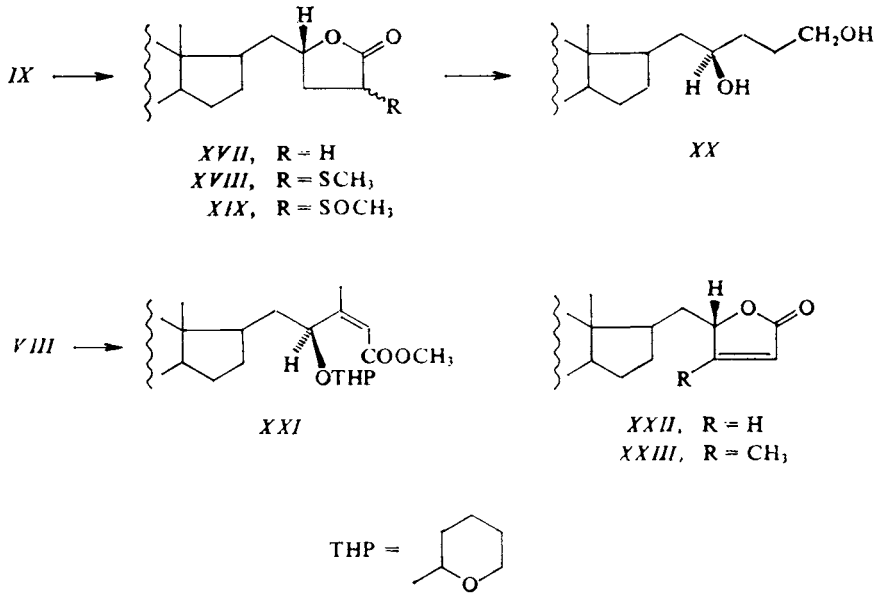
Hydrogenation of the unsaturated hydroxy ester *V* over palladium on charcoal afforded the corresponding saturated hydroxy ester which was converted into the lactone *X* by treatment with perchloric acid in tetrahydrofuran. In the analogous way, the lactone *XVII* was prepared from the unsaturated ester *IX*. The lactones *X* and *XVII* were reduced with sodium bis(2-methoxyethoxy)aluminium hydride to give the known[1] diols *XIII* (configuration 22*S*) and *XX* (configuration 22*R*), respectively. This shows the respective configurations 22*S* and 22*R* for the lactone *X* and *XVII*; 22*R*-configuration for the acetylenic derivatives *II*–*V* and 22*S*-configuration for the derivatives *IV*–*IX*. For the preparation of the unsaturated lactones *XV* and *XXII* we applied a sulfenylation and dehydrosulfenylation method[4,5] to the respective saturated lactones *X* and *XVII*.

Reaction of the lactone *X* with lithium diisopropylamide gave the corresponding anion which on reaction with dimethyl disulfide afforded α-methylthiolactone *XI*. This was oxidized with *m*-chloroperoxybenzoic acid at −78°C to give α-methylsulfinyl lactone *XII* from which the unsaturated lactone *XV* was obtained in 68%



overall yield by heating with calcium carbonate in toluene. The unsaturated lactone *XXII* was prepared in 66% overall yield from the lactone *XVII* in the same way *via* the intermediates *XVIII* and *XIX*. The structure of the lactone *XV* was confirmed by its IR spectrum which contained bands at 1 779 and 1 763 cm^{-1}, characteristic of an α,β-unsaturated five-membered lactone ring. Its ^1H NMR spectrum exhibits $C_{(22)}$—H proton signals as a multiplet at $\delta = 5{\cdot}02$ and $C_{(23)}$—H and $C_{(24)}$—H proton signals as doublets of doublets, the found coupling constants $J_{23,24} = 5{\cdot}6$ Hz, $J_{22,23} = 1{\cdot}5$ Hz and $J_{22,24} = 2$ Hz agreeing with values found previously for similar compounds[5,6]. The spectral parameters of the isomeric lactone *XXII* are practically identical. Also the CD spectra of the lactones *XV* and *XXII* at 215 nm are practically enantiomorphous. The negative Cotton effect ($\Delta\varepsilon$ −8·77) of the lactone *XV* indicates[7] the absolute configuration 22*R* whereas the positive effect of the lactone *XXII* ($\Delta\varepsilon$ +8·97) shows a 22*S* configuration[7], these results being in accord with the configuration of the starting saturated lactones *X* and *XVII*.

The acetylenic esters *IV* and *VIII* are suitable starting compounds for the preparation of β-substituted α,β-unsaturated lactones. Reaction of the ester *IV* with lithium dimethylcuprate[2] gave the unsaturated ester *XIV*. Its ^1H NMR spectrum shows signal of a methyl at a double bond at $\delta = 1{\cdot}82$ and a signal due to one olefinic proton at $\delta = 5{\cdot}74$ which proves the addition of the organocopper reagent to the triple bond in the ester *IV*. In the next step, the ester *XIV* was treated with dilute hydrochloric acid in a methanol–acetone–benzene mixture which removed the tetrahydropyranyl protecting group and closed the lactone ring under formation of the unsaturated lactone *XVI*. Its structure is confirmed by the IR spectral bands at 1 758,



1 745 and 1 643 cm^{-1}, characteristic of an unsaturated five-membered lactone. The ^1H NMR spectrum displays a multiplet at $\delta = 4{\cdot}79$ due to the $C_{(22)}$—H proton, a pentet of $C_{(24)}$—H at $\delta = 5{\cdot}78$ ($J = 1{\cdot}5$ Hz) and a doublet of doublets at $\delta = 2{\cdot}03$ due to the $C_{(23)}$—CH_3 methyl ($J = 1{\cdot}5$ and $0{\cdot}6$ Hz). According to the decoupling experiments, the $C_{(22)}$—H proton interacts with $C_{(23)}$—H proton ($^4J = 0{\cdot}6$ Hz) and with $C_{(24)}$—H proton (allylic $J = 1{\cdot}5$ Hz), the $C_{(24)}$—H proton interacts with the $C_{(22)}$—H proton (allylic $J = 1{\cdot}5$ Hz) and with $C_{(23)}$—CH_3 (allylic $J = 1{\cdot}5$ Hz), and the $C_{(23)}$—CH_3 methyl protons interact with the $C_{(22)}$—H and $C_{(24)}$—H protons ($^4J = 0{\cdot}6$ Hz and allylic $J = 1{\cdot}5$ Hz, respectively). The values of the allylic coupling constants agree with those observed previously[8] for 4,4-disubstituted derivatives of 3-methyl-2-buten-1→4-olide. The same procedure was employed in the preparation of the unsaturated lactone *XXIII* from the acetylenic ester *VIII via* the intermediate *XXI*. According to the CD spectra[7], the lactone *XVI* ($\Delta\varepsilon$ −10·20 at 210 nm) has configuration 22*R* and the lactone *XXIII* ($\Delta\varepsilon$ +3·95 at 212 nm) configuration 22*S* which is in accord with the configurations derived for the starting acetylenic esters *IV* and *VIII*.

EXPERIMENTAL

Melting points were determined on a Kofler block (Boetius, G.D.R.). Optical rotations were measured in chloroform at 25°C on a Perkin–Elmer 141 MC instrument and are given in 0·01 deg . . kg^{-1} m^2, IR spectra were taken on a Perkin–Elmer 580 spectrometer (wavenumbers given

in cm^{-1}), CD spectra were measured on a Dichrographe II (Roussel–Jouan) instrument. Mass spectra were taken on an AEI 901 spectrometer. Column chromatography was performed on silica gel (Pitra, 60—120 μm) or on neutral alumina (Reanal, grade II). Thin-layer chromatography (TLC) was carried out on silica gel G according to Stahl (Woelm), preparative TLC was done on 200 × 200 × 0·7 mm plates. Prior to evaporation *in vacuo* at about 2 kPa, the solutions in organic solvents were dried over anhydrous sodium sulfate. Analytical samples were dried

TABLE I

Characteristic parameters of ^{1}H NMR spectra

Compound[a]	$C_{(18)}$—H_3	$C_{(19)}$—H_3	$C_{(22)}$—H	$C_{(23)}$—H	$C_{(24)}$—H
II	0·57 s	0·77 s	4·34 . W = 25 Hz	—	2·45 d[b]
III[c]	0·57 s	0·77 s	4·42 m $W \approx$ 20 Hz	—	2·39 d[b]
IV[d]	0·57 s	0·77 s	4·53 m	—	—
V[e]	0·57 s	0·77 s	4·44 m W = 25 Hz	—	—
VI	0·57 s	0·77 s	4·31 m W = 25 Hz	—	2·45 d[b]
VII[f]	0·58 s	0·78 s	4·36 m	—	2·34 d[b]
VIII[d]	0·57 s	0·77 s	4·54 m	—	—
IX[e]	0·57 s	0·77 s	4·46 m $W \approx$ 20 Hz	—	—
X	0·55 s	0·77 s	4·43 m $W \approx$ 30 Hz	[g]	2·44 m[h]
XIV[i]	0·53 s	0·77 s	[g]	—	5·74 bs
XV	0·57 s	0·77 s	5·02 m W = 18 Hz	7·44 dd[j]	6 08 dd[k]
XVI[l]	0·56 s	0·76 s	4·79 W = 15 Hz	—	5·78 p[m]
XVII	0·56 s	0·77 s	4·48 m $W \approx$ 30 Hz	[g]	2·44 m[h]
XXI[n]	0·57 s	0·77 s	[g]	—	5·83 bs
XXII	0·57 s	0·77 s	5·03 m W = 19 Hz	7·47 dd[o]	6·08 dd[p]
XXIII[q]	0·57 s	0·76 s	4·82 m W = 15 Hz	—	5·77 p[m]

[a] The spectra were measured in deuteriochloroform with tetramethylsilane as internal standard on a Tesla BS-467 (60 MHz) instrument. Chemical shifts are given in ppm (δ-scale). All values were obtained by first order analysis. [b] $J_{22,24}$ = 2·1 Hz. [c] Further signals: 2·43 d, J = 2·1 Hz $C_{(24)}$—H of the side-product; 4·71 bs $C_{(2)}$—H of the tetrahydropyranyloxy group of the side-product; 4·97 bs $C_{(2)}$—H of of tetrahydropyranyloxy group of the principal product; ratio of isomers 85 : 15 (integration of the signals). [d] Other signals: 3·76 s $COOCH_3$; 4·90 bs $C_{(2)}$—H of the tetrahydropyranyloxy group. [e] Other signal 3·76 s $COOCH_3$. [f] Other signals: 2·42 d J = 2·1 Hz $C_{(24)}$—H of the side-product; 4·75 bs $C_{(2)}$—H of tetrahydropyranyloxy group of the side-product; 4·97 bs 2-H of tetrahydropyranyloxy group of the principal product; isomer ratio 80 : 20 (integration of signals). [g] Undeterminable value. [h] Signal intensity 2 H. [i] Other signals: 1·82 d J = 1·2 Hz ($C_{(23)}$—CH_3); 3·67 s $COOCH_3$; 4·37 bs $C_{(2)}$—H of tetrahydropyranyloxy group. [j] $J_{22,23}$ = 1·5 Hz, $J_{23,24}$ = 5·6 Hz, [k] $J_{22,24}$ = 2 Hz, $J_{23,24}$ = 5·6 Hz. [l] Other signal: 2·03 dd J = 1·5 + 0·6 Hz ($C_{(23)}$—CH_3). [m] J = 1·5 Hz. [n] Other signals: 1·79 d J = 1·3 Hz $C_{(23)}$—CH_3; 3·67 s $COOCH_3$; 4·42 bs $C_{(2)}$—H of tetrahydropyranyloxy group. [o] $J_{22,25}$ = = 1·4 Hz, $J_{23,24}$ = 5·6 Hz. [p] $J_{22,24}$ = 1·8 Hz; $J_{23,24}$ = 5·6 Hz. [q] Other signals: 2·08 dd J = = 1·5 + 0·6 Hz ($C_{(23)}$—CH_3).

at 50°C and 26 Pa for 12 h. The identity of compounds was confirmed by comparison of their IR and ^{1}H NMR spectra, thin-layer chromatography and mixture melting points.

(22*R*)-21-Nor-5α-chol-23-yn-22-ol (*II*)

A solution of ethylmagnesium bromide in tetrahydrofuran (8·5 ml, *c* 0·85 mol l^{-1}) was added to tetrahydrofuran (10 ml) which had been saturated with acetylene at 0°C. After introduction of dry acetylene into the mixture for 30 min, a solution of the aldehyde *I* (ref.[1], 450 mg; 1·49 mmol) in tetrahydrofuran (6 ml) was added and the acetylene was bubbled into the mixture for further 20 min. The mixture was stirred at room temperature for 2 h, cooled to 0°C and a saturated aqueous solution of ammonium chloride (100 ml) was added. The product was taken up in ether, the extract washed with ammonium chloride solution and taken down. The residue was chromatographed preparatively on 10 plates of silica gel in ether–light petroleum (15 : 85; twice developed). Zones, containing the less polar compound, were combined and eluted with ether, affording 155 mg (32%) of the acetylenic derivative *II*, m.p. 108—110°C (light petroleum), $[\alpha]_D$ +32° (*c* 1·2); IR spectrum (tetrachloromethane): 3 310, 2 110 (C≡C—H), 3 620, 1 049, 1 020 (OH). Mass spectrum, *m/z*: 328 (M^+), 313 (M—CH_3), 310 (M—H_2O), 295 (M—CH_3—H_2O). For $C_{23}H_{36}O$ (328·5) calculated: 84·09% C, 11·04% H; found: 83·81% C, 11·01% H.

Methyl (22*R*)-22-Hydroxy-21,26,27-trinor-5α-cholest-23-yn-25-oate (*V*)

A) Dihydropyrane (0·1 ml; 1·1 mmol) and *p*-toluenesulfonic acid monohydrate (3 mg) were added to a solution of the alcohol *II* (133 mg; 0·40 mmol) in dichloromethane (5 ml). After stirring at room temperature for 2 h, the mixture was diluted with light petroleum (30 ml) and applied on a column of alumina (20 g). Elution with ether–light petroleum (2 : 98) gave 140 mg (84%) of the oily product *III* which, according to TLC (ether–light petroleum 1 : 9), was a mixture of a principal product of R_F 0·74 and a minor product of R_F 0·64. A solution of 1-butyllithium in hexane (0·37 ml; *c* 1·6 mol l^{-1}) was added under argon at −78°C to the compound *III* (120 mg; 0·29 mmol) in tetrahydrofuran (3 ml). After stirring for 15 min, methyl chloroformate (0·05 ml; 0·65 mmol) was added, the mixture was allowed to attain 0°C and was stirred at this temperature for 1 h. The mixture was decomposed with saturated aqueous solution of ammonium chloride, the product was extracted with ether and the extract was washed with ammonium chloride solution. Evaporation of the solvents *in vacuo* afforded 165 mg of an oily product *IV* which, according to TLC in ether–light petroleum (1 : 9), consisted of two principal products of R_F 0·48 (more intensive spot) and 0·37 (less intensive spot). A solution of the crude product *IV* (145 mg) in a mixture of benzene (3 ml) and methanol (9·5 ml) was stirred with water (0·5 ml) and *p*-toluenesulfonic acid monohydrate (25 mg) at room temperature for 20 h. The solvents were evaporated *in vacuo*, the residue was dissolved in ether, the ethereal solution was washed with saturated aqueous solution of potassium hydrogen carbonate and with water and taken down. Chromatography of the residue on a column of silica gel (17 g) in ether–light petroleum (10 : 90) afforded 76 mg (64% based on the alcohol *II*) of the ester *V*, m.p. 81—84°C (light petroleum); $[\alpha]_D$ +29° (*c* 1·7). IR spectrum (tetrachloromethane): 3 612, 3 415 (OH), 2 238 (C≡C), 1 721, 1 250 ($COOCH_3$). For $C_{25}H_{38}O_3$ (386·6) calculated: 77·68% C, 9·91% H; found: 77·53% C, 10·20% H.

B) A solution of 1-butyllithium in hexane (5·4 ml, *c* 1·6 mol l^{-1}) was added at −78°C in the course of 10 min to a stirred solution of diisopropylamine (873 mg; 8·63 mmol) in tetrahydrofuran (10 ml) under argon. The temperature was kept at −78°C for 30 min and methyl propiolate (0·82 ml; 9·22 mmol) was added during 10 min. After stirring for additional 80 min at −78°C, a solution of the aldehyde *I* (ref.[1]; 900 mg, 2·98 mmol) in tetrahydrofuran (10 ml) was added and the mixture was stirred for 2 h more at −78°C under argon. Solid ammonium chloride (2 g)

and water (5 ml) were added, the mixture was left to achieve room temperature, diluted with saturated aqueous ammonium sulfate and the product was taken up in ether. The extract was washed with solutions of ammonium sulfate, potassium hydrogen carbonate and ammonium sulfate, dried and taken down. The residue was chromatographed on 16 plates of silica gel in benzene–ether (95 : 5, twice developed). Zones, containing the less polar compound, were combined and eluted with ether, giving 262 mg (23%) of the ester *V*, m.p. 82–85°C (light petroleum), identical with a sample prepared under *A*).

(22*S*)-21-Nor-5α-chol-23-yn-22-ol (*VI*)

The thin-layer chromatographic zones of the more polar compound in the preparation of the alcohol *II* were combined and eluted with ether affording 155 mg (32%) of the alcohol *VI*, m.p. 106–108°C (light petroleum), $[\alpha]_D$ +30° (*c* 1·2). IR spectrum (tetrachloromethane): 3 615, 1 019 (OH), 3 310, 2 110 (C≡C—H); mass spectrum, *m/z*: 328 M^+, 313 (M−CH_3), 310 (M−H_2O), 295 (M−CH_3—H_2O). For $C_{23}H_{36}O$ (328·5) calculated: 84·09% C, 11·04% H; found: 83·79% C, 11·25% H.

Methyl (22*S*)-22-Hydroxy-21,26,27-trinor-5α-cholest-23-yn-25-oate (*IX*)

A) The alcohol *VI* (133 mg; 0·40 mmol) was converted into the derivative *VII* in the same manner as the compound *III* from *II* (described in the preparation of *V*, procedure *A*), yield 141 mg (84%). The obtained product was shown by TLC (ether–light petroleum 1 : 9) to be a mixture of two isomers: a main product of R_F 0·72 and a minor one of R_F 0·62. The ester *IX* was prepared from compound *VII* (120 mg; 0·29 mmol) as described for the ester *V*; yield 75 mg (64% based on *VI*) of *IX*, m.p. 129–132°C (light petroleum), $[\alpha]_D$ +30° (*c* 1·7). IR spectrum (tetrachloromethane): 3 617, 3 450 (OH), 2 238 (C≡C), 1 721, 1 250 ($COOCH_3$). For $C_{25}H_{38}O_3$ (386·6) calculated: 77·68% C, 9·91% H; found: 77·66% C, 10·05% H.

B) The thin-layer chromatographic zones of the more polar compound in the preparation of the ester *V* (method *B*) were combined and eluted with ether, affording 265 mg (23%) of the ester *IX*, m.p. 131–134°C (light petroleum), identical with the sample prepared according to *A*).

(22*S*)-21,26,27-Trinor-5α-cholestan-25→22-olide (*X*)

The ester *V* (155 mg; 0·40 mmol) was hydrogenated in ethyl acetate (15 ml) over a 10% palladium-on-carbon catalyst (30 mg) at atmospheric pressure and room temperature for 1 h. The catalyst was filtered off, washed with ethyl acetate, and the filtrate was taken down. The residue was dissolved in tetrahydrofuran (15 ml) and mixed with 70% perchloric acid (2 drops). After standing for 15 min at room temperature, the mixture was diluted with ether (200 ml), washed with potassium hydrogen carbonate solution and water, the solvent was evaporated and the residue chromatographed on a column of silica gel (20 g). Elution with light petroleum–benzene–ether (48 : 48 : 4) gave 108 mg (75%) of the lactone *X*, m.p. 123–125°C (light petroleum), $[\alpha]_D$ +43° (*c* 1·9). IR spectrum (tetrachloromethane): 1 780, 1 179 (γ-lactone); CD spectrum (dioxane): 215 nm (Δε −0·27). For $C_{24}H_{38}O_2$ (358·6) calculated: 80·39% C, 10·68% H; found: 80·18% C, 10·95% H.

(22*S*)-21,26,27-Trinor-5α cholestane-22,25-diol (*XIII*)

Sodium bis(2-methoxyethoxy)aluminium hydride (0·3 ml of 70% benzene solution) was added to a solution of the lactone *X* (30 mg; 0·083 mmol) in benzene (5 ml). After stirring and refluxing for 2 h under argon, the mixture was decomposed with methanol and diluted with ether (100 ml).

The ethereal solution was washed with dilute (1 : 4) hydrochloric acid, water, saturated potassium hydrogen carbonate solution and water, and the solvent was evaporated. Crystallization of the residue from ether–light petroleum afforded 23 mg (82%) of the diol *XIII*, m.p. 119–121°C, identical with an authentic sample[1].

(22*R*)-21,26,27-Trinor-5α-cholest-23-en-25→22-olide (*XV*)

A solution of 1-butyllithium in hexane (0·8 ml; 1·6 mol l^{-1}) was added at −78°C to a stirred solution of diisopropylamine (126 mg; 1·25 mmol) in tetrahydrofuran (2 ml) under argon. After 15 min a solution of *X* (125 mg; 0·35 mmol) in tetrahydrofuran (3 ml) was added. The mixture was allowed to attain room temperature during 30 min and then dimethyl disulfide (105 mg; 1·12 mmol) was added. After stirring at room temperature for 1 h the mixture was poured into dilute hydrochloric acid, the product was extracted with ether and the extract was washed with a potassium hydrogen carbonate solution and water. After evaporation of the solvent, the residue was dissolved in dichloromethane (10 ml), cooled to −78°C and a solution of *m*-chloroperoxybenzoic acid (71 mg; 85% purity; 0·35 mmol) in dichloromethane (1 ml) was added dropwise. After stirring at −78°C for 10 min, the mixture was poured into 10% aqueous solution of sodium thiosulfate, the product was extracted with ether, the extract was washed with potassium hydrogen carbonate solution and water and taken down. The residue was dissolved in toluene (25 ml), calcium carbonate (500 mg) was added and the stirred mixture was refluxed under argon for 4 h. After filtration through Celite and evaporation, the residue was chromatographed on two preparative plates of silica gel in light petroleum–benzene–ether (45 : 45 : 10), affording 85 mg (68%) of the unsaturated lactone *XV*, m.p. 137–140°C (ether–light petroleum), $[\alpha]_D$ −18° (*c* 1·5). IR spectrum (tetrachloromethane): 1 779, 1 763 (unsaturated γ-lactone); CD spectrum (dioxane): 215 nm (Δε −8·77). For $C_{24}H_{36}O_2$ (356·6) calculated: 80·85% C, 10·18% H; found: 81·14% C, 10·14% H.

(22*R*)-23-Methyl-21,26,27-trinor-5α-cholest-23-en-25→22-olide (*XVI*)

A solution of methyllithium in ether (4 mol, 0·85 mol l^{-1}) was added at −22°C under argon to a stirred suspension of copper (*I*) iodide (322 mg; 1·69 mmol) in ether (6 ml). The mixture was cooled to −78°C and a solution of the ester *IV* (prepared from 330 mg (1 mmol) of *II*; see the preparation of *V*, method *A*) in ether (6 ml) was added. After stirring at −78°C for 3 h, the mixture was decomposed with methanol (2·2 ml) and warmed to 0°C. Saturated aqueous ammonium chloride solution (15 ml) was added, the mixture was stirred at 0°C for 30 min, extracted with ether and the extract was washed with an ammonium chloride solution and taken down. Crystallization from methanol gave a sample of the ester *XIV*. The combined mother liquors were taken down, the residue dissolved in a mixture of methanol (10 ml), acetone (30 ml) and benzene (20 ml) and warmed to 40°C with dilute hydrochloric acid (1 : 4; 10 ml) for 12 h with stirring. The mixture was diluted with ether (150 ml) and the ethereal layer was washed successively with saturated aqueous solutions of ammonium sulfate, potassium hydrogen carbonate and ammonium sulfate. The solvent was evaporated and the residue crystallized from light petroleum–dichloromethane to give 205 mg (55%) of the unsaturated lactone *XVI*, m.p. 201 to 202°C; $[\alpha]_D$ +2° (*c* 2·5). IR spectrum (chloroform): 1 758, 1 745, 1 643 (unsaturated γ-lactone); CD spectrum (dioxane): 210 nm (Δε −10·20). For $C_{25}H_{38}O_2$ (370·6) calculated: 81·03% C, 10·34% H; found: 80·78% C, 10·23% H.

(22*R*)-21,26,27-Trinor-5α-cholestan-25→22-olide (*XVII*)

The title lactone was prepared from the ester *IX* (155 mg; 0·40 mmol) in the same manner as described for the lactone *X* from the ester *V*; yield 113 mg (79%) of *XVII*, m.p. 156–158°C

(hexane), $[\alpha]_D$ +6° (*c* 1·9). IR spectrum (tetrachloromethane): 1 780, 1 179 (γ-lactone); CD spectrum (dioxane): 215 nm ($\Delta\varepsilon$ +0·49). For $C_{24}H_{38}O_2$ (358·6) calculated: 80·39% C, 10·68% H; found: 80·68% C, 10·63% H.

(22*R*)-21,26,27-Trinor-5α-cholestane-22,25-diol (*XX*)

The diol *XX* was prepared from the lactone *XVII* (30 mg; 0·083 mmol) as described for the preparation of *XIII* from *X*. Crystallization from ether–light petroleum afforded 22 mg (78%) of the diol *XX*, m.p. 144–146°C, identical with an authentic sample[1].

(22*S*)-21,26,27-Trinor-5α-cholest-23-en-25→22-olide (*XXII*)

The title compound was prepared from the lactone *XVII* (125 mg; 0·35 mmol) *via* the intermediates *XVIII* and *XIX* in the same way as described for the preparation of the lactone *XV* from lactone *X*. The obtained unsaturated lactone *XXII* (82 mg; 66%) melted at 118–121°C (light petroleum); $[\alpha]_D$ +66° (*c* 2·1). IR spectrum (tetrachloromethane): 1 775 sh, 1 764 (unsaturated γ-lactone); CD spectrum (dioxane): 215 nm ($\Delta\varepsilon$ +8·97). For $C_{24}H_{36}O_2$ (356·6) calculated: 80·85% C, 10·18% H; found: 80·78% C, 9·89% H.

(22*S*)-23-Methyl-21,26,27-trinor-5α-cholest-23-en-25→22-olide (*XXIII*)

The lactone *XXIII* was prepared from the ester *VIII* (prepared from 330 mg (1 mmol) of the alcohol *VI* as described for *IX*, procedure *A*) in the same way as the lactone *XVI* from the ester *IV*. Crystallization from light petroleum–dichloromethane gave 158 mg (43%) of the unsaturated lactone *XXIII*, m.p. 196–198°C; $[\alpha]_D$ +11° (*c* 2·1). IR spectrum (chloroform): 1 758, 1 743, 1 643 (unsaturated γ-lactone); CD spectrum (dioxane): 212 nm ($\Delta\varepsilon$ +3·95); mass spectrum, *m/z*: 370 (M^+). For $C_{25}H_{38}O_2$ (370·6) calculated: 81·03% C, 10·34% H; found: 81·21% C, 10·61% H.

The analyses were carried out in the Analytical Laboratory of this Institute (Dr J. Horáček, Head). The IR *and* CD *spectra were recorded and interpreted by Dr S. Vašíčková,* ^{1}H NMR *spectra were recorded by Mrs J. Jelínková and Mrs M. Snopková. For the decoupling experiments we are indebted to Dr M. Masojídková. The mass spectra were measured and interpreted by Dr A. Trka.*

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